THE American Journal OF Gastroenterology

VOL. 28, NO. 5 NOVEMBER, 1957

Management of Peptic Ulcer with Unrestricted Diet and a New Combination of Therapeutic Agents

A Simple Method for Improving Visualization of the Hypermotile Stomach and Duodenal Bulb

The Timed Integration of Stool Hydration and Peristaltic Stimulation in Constipation Correction

The Diagnosis and Treatment of Chronic Regional Enteritis

Twenty-third Annual Convention
New Orleans, Louisiana
19, 20, 21, 22 October 1958

Official Publication
AMERICAN COLLEGE
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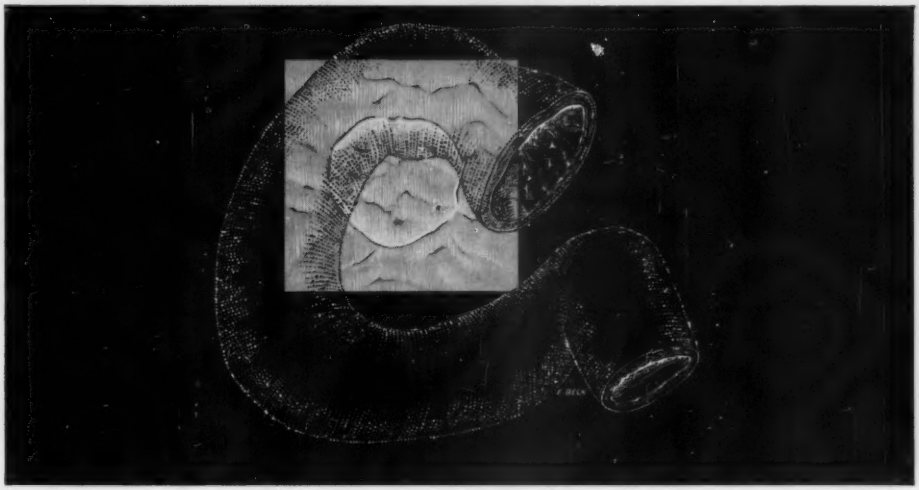

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1. Lichstein, J.; Morehouse, M. G., and Osmon, K. L.: Am. J. M. Sc. *232*:156 (Aug.) 1956.

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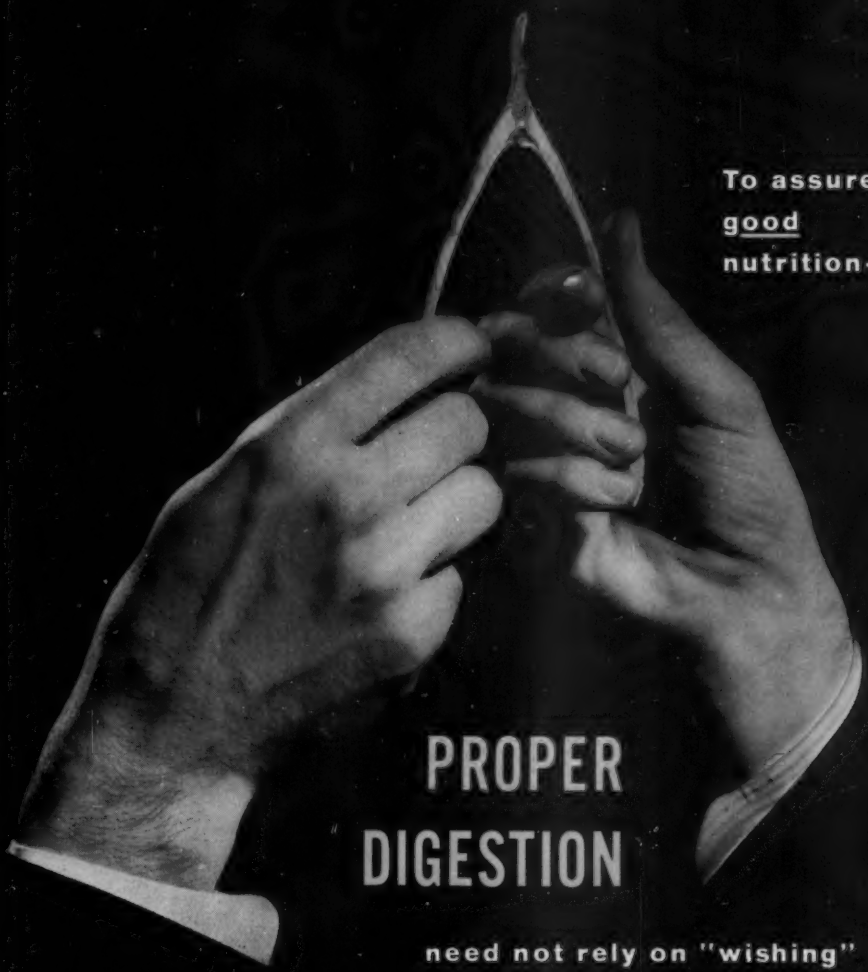

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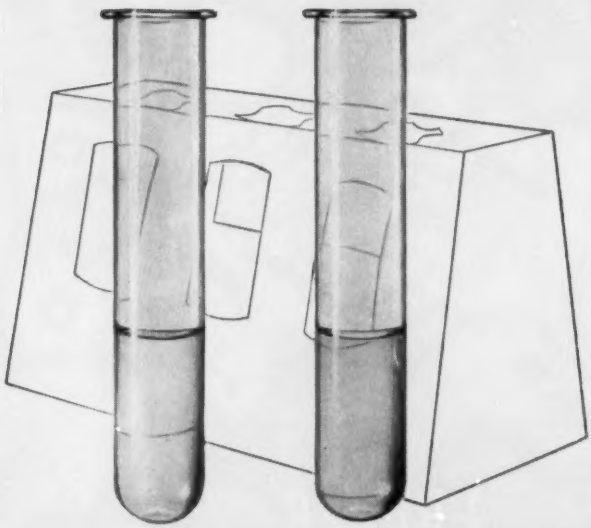

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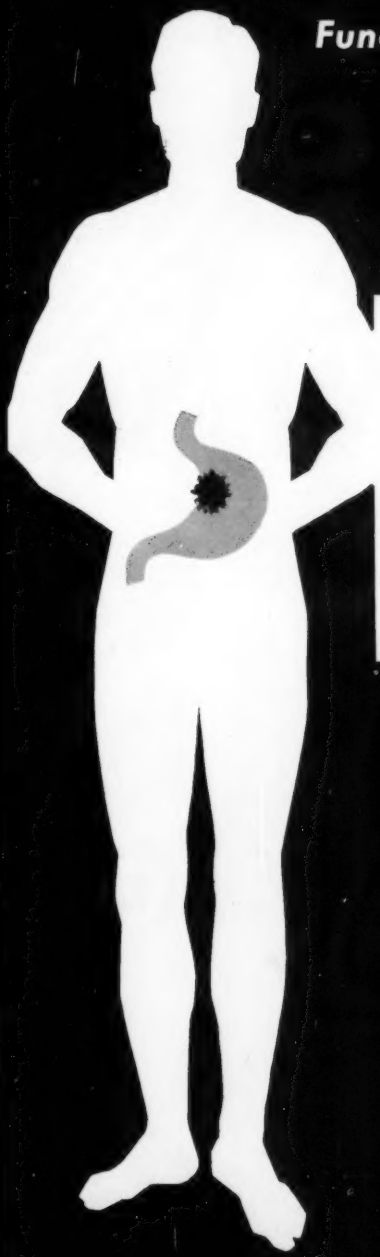

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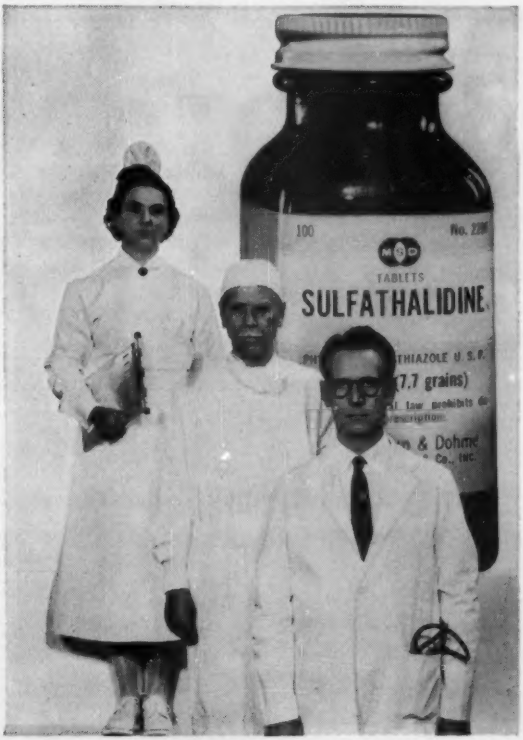

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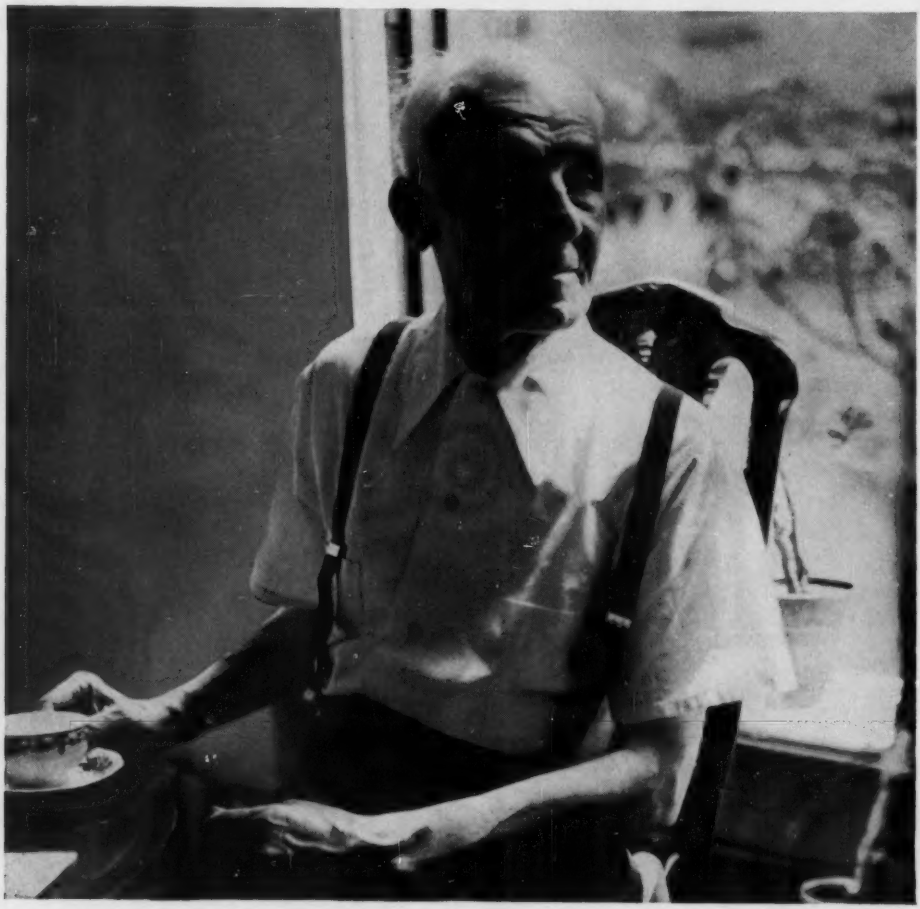

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VOLUME 28 NOVEMBER, 1957 NUMBER 5

MANAGEMENT OF PEPTIC ULCER WITH UNRESTRICTED DIET AND A NEW COMBINATION OF THERAPEUTIC AGENTS

LOUIS A. ROSENBLUM, M.A., M.D., F.A.C.P., F.A.C.G.
Forest Hills, N. Y.

The role of nutrition in the management of peptic ulcer has been explored by many investigators. From the promulgation of the first dietary regimen—the "milk diet" of Cruveilhier[1]—the time-honored method of treatment has involved use of a limited, bland diet restricted to milk and milk products. That it had nutritional and other disadvantages is amply attested by the numerous variations and modifications that subsequently appeared in the literature. The merit of such a diet has been questioned by numerous investigators, but the regimen has remained in use since it is believed to cause less irritation and secretory stimulation, and presumably possesses more acid-absorbing properties. In general, patients on such diets usually are satisfactorily relieved of pain.

Recent advances in our knowledge of nutrition and of the psychogenic aspects of peptic ulcer, however, have tended to cast considerable doubt on the efficacy of any restricted diet in the management of peptic ulcer. It is now becoming evident that the traditional bland dietary has many disadvantages. The importance of the B vitamins and Vitamin C in the healing of wounds is well known. Studies have indicated that the level of Vitamin C is low in the blood and urine of patients with peptic ulcer in comparison with blood and urine levels of this vitamin in normal individuals[2]. Rosenblum and Jolliffe have demonstrated that deficiency of the water-soluble vitamins may occur in patients with peptic ulcer as the result of a dual mechanism caused by 1. deficient vitamin intake from the restricted ulcer diets and 2. inactivation and adsorption by the alkalis and surface-active antacids that are used in large amounts in such diets[3].

Another important element—iron—is deficient in milk and milk products. Insufficiency of this mineral contributes to impairment of healing. The serum protein level also is low in individuals with peptic ulcer. The usual Sippy regimen and its modifications are deficient in protein. This, too, favors interference

with healing. Furthermore, the Sippy diet if maintained for a long period may aid in recurrence of the ulcer.

Milk sensitivity occasionally prevents subsidence of pain on a restricted diet. In fact, it is not unusual to find that many individuals cannot tolerate large quantities of milk or milk products without pain and other nonspecific gastrointestinal symptoms. Occasionally, in some patients, milk will form large indigestible curds in the stomach, with resulting increase of pain and gastric discomfort.

Investigations into the etiology and pathogenesis of atherosclerosis have brought into prominence the dietary aspects of treatment and prevention of early vascular sclerosis. Such prophylactic regimens employ diets high in protein and low in cholesterol and animal fats. In a patient suffering from peptic ulcer with hypercholesterolemia (and these are numerous in the arteriosclerotic age group) the vascular status would be jeopardized if he were to adhere to a strict type of Sippy regimen, which is characterized by a relatively high fat, low protein content. For such a patient, treatment of the peptic ulcer must be based on a regimen that will not increase the vascular damage. Therefore a free or regular diet must be used.

Another situation in which adherence to a strict ulcer diet may aggravate or even initiate other pathological processes is in the presence of gallbladder disease coexistent with peptic ulcer. This is not a rare condition. To the contrary, it is found often enough to warrant serious consideration. In patients with fat intolerance, biliary dyskinesia or other functional gallbladder syndrome, administration of the relatively high fat peptic ulcer diet is apt to exacerbate the biliary condition, so that the clinical picture may resemble that of a refractory ulcer or a confusing pain pattern. These patients should be treated with a diet designed for the gallbladder disturbance, and not primarily for the peptic ulcer, which should be managed with a free choice of foods.

It is generally agreed that there is a tremendous *psychogenic factor* in the etiology and development of peptic ulcer, regardless of specific psychodynamic pathways or of differences in the so-called "ulcer profiles". Peptic ulcer represents a true psychosomatic disease. Consequently, all psychological factors must be taken into consideration, not only in determining the pathogenesis of the ulcer but, more important, in the treatment and prevention of recurrences and complications. The patient with an ulcer is not concerned with theories and the like. He wants quick relief from his pain, and he wants it with a minimum of inconvenience and disturbance of his daily routine. Comparison of therapeutic management by bed rest with management by ambulatory treatment in ulcer patients proved that the end results of the ambulatory method were superior to those obtained by hospitalization. There were many explanations for this finding but one outstanding reason was that mental reassurance is of more significance than physical rest when the patient is under economic or other stress[4].

One must bear in mind that a diagnosis of peptic ulcer already carries a tremendous threat to the security of the individual. The treatment encompasses care of the total individual, not simply a small localized area of destruction in the gastric or duodenal mucosa[5]. Therefore, imposition of the usual ulcer regimen with restricted diet, frequent feedings, and frequent medication is tantamount to adding insult to injury. To a tension-ridden individual who is already under a threat when the diagnosis is disclosed, we then add the additional burden of insecurity and strain caused by disruption of his regular routine when he embarks on the regimen usually prescribed.

Since abatement of ulcer symptoms is not necessarily synonymous with healing or even cure, despite radiologic disappearance of the crater, we are faced with the necessity for continuous therapy over prolonged intervals, possibly three to six or nine months and even longer. In fact, it is felt that in many ulcer patients antiulcer measures must be maintained on a permanent basis to prevent recurrences and complications[6]. It is obvious that the vast majority of patients would not long adhere to any cumbersome and annoying regimen of restricted diet and medication. In fact, it is a common experience to find that most patients, regardless of all attempts to indoctrinate them in the nature of the disease and the necessity for prolonged and intensive treatment, would abandon the conventional therapeutic measures as soon as a reasonable amount of relief was secured. It was, therefore, decided to investigate the efficacy of a regimen designed to permit the patient to obtain relief of symptoms and favor healing of the ulcer, meanwhile employing a full diet of free choice and medication that may be administered in an easy and convenient manner. Such a regimen would stimulate less resistance on the part of the patient to prolonged and even continuous treatment.

Unlimited diet in the treatment of peptic ulcer has been successfully used by many investigators. Marshall has reported statistics on the treatment of a large group of patients with an unrestricted diet. He, however, used large amounts of an antacid-antispasmodic preparation that was taken in tablet form every two hours during the daytime and also had to be administered during the night. A minimum of four to six months of treatment was required[7,8]. The disadvantage of medication every two hours and through the night is obvious.

Other series have been reported in which treatment with unlimited diet was employed, and smoking and alcoholic beverages were permitted. Intensive psychotherapeutic measures during hospitalization supplemented the dietary regimen. Patients treated in this manner became asymptomatic more quickly than did controls on conventional diet and routine medication with antacids and antispasmodics[9]. We do not, however, know the follow-up results when psychotherapy was discontinued.

A more recent study on hospitalized and ambulatory patients with both gastric and duodenal ulcers demonstrated that the rate of healing of a gastric

ulcer was not materially affected by limiting the diet to bland foods[10]. The ambulatory patients on a regular diet in this series more nearly approached our aim, and apparently these did well over a period of about a year.

Method

This paper presents the results of a two-fold investigation: 1. the antiulcer effectiveness of a more rational therapeutic combination of antacids, anticholinergic agent and Vitamin C; and 2. the use of this preparation without dietary restrictions in the treatment of ulcer patients. The antacid-antispasmodic preparation was in tablet form and consisted of aluminum hydroxide, 200 mg.; magnesium oxide, 50 mg.; scopolamine methylbromide or methylnitrate, 2 mg., and ascorbic acid, 10 mg.* This will be referred to as tablet P.

The use of aluminum hydroxide and magnesium oxide as antacids needs no discussion here. The accepted use of these substances almost as agents of choice for effectiveness and virtual absence of reactions and side-effects is attested to in virtually the entire literature. The choice, however, of an antisecretory drug has not been so nearly unanimous. Ever since the need of a gastric secretory depressant was first realized and atropine was used, there has been a continuous search for new and more potent anticholinergic drugs. Many have been tried and discarded because of relative ineffectiveness, and, more important, the frequent incidence of side-effects when administered in therapeutic amounts. A re-evaluation of some of the older drugs has demonstrated that scopolamine methylbromide satisfactorily fills the requirements of an effective oral anticholinergic. The publication of Sun[11], Rider[12], and Kirsner[13] demonstrate the usefulness of scopolamine methylbromide by mouth for peptic ulcer, with prolonged action and relative freedom from annoying or disabling side reactions. Lastly, ascorbic acid was included to overcome the Vitamin C deficiency common to peptic ulcer patients[14] and to facilitate healing of the ulcer.

One hundred forty-five patients with clinical and roentgen diagnosis of peptic ulcer were treated with tablet P and a normal unrestricted diet. All but three were managed on an ambulatory basis and were permitted to continue their usual occupations. The three exceptions were hospitalized for hemorrhage and were treated in the usual manner until active bleeding had ceased. They were then permitted a full unrestricted diet and given tablet P. Treatment was continued without interruption from four to twenty months.

Follow-up roentgenograms were taken at intervals of one to three months. All patients were seen every two to six weeks throughout the study. Since this was to be a clinical study and it was felt that determinations of gastric acidity would contribute little to the ultimate result, gastric analysis was not performed.

*The tablets employed in this study (Pepulcin® Tablets) were supplied by Ives-Cameron Company.

The history of ulcer in these patients varied from one month to eighteen years. The majority had had numerous recurrences and therefore experiences with many other types of treatment and diet. Accordingly it was felt that these patients would act as their own controls.

The patients studied were grouped as follows:

Types of Ulcers:	Duodenal	134
	Gastric	8
	Pyloric	2
	Marginal	1
	Total	145
Sex Distribution:	Males—90	Females—55
Age Distribution:	Male: 26-71 years	Female: 24-69 years

Dosage:—With many of the commonly used anticholinergic and antispasmodic drugs in full therapeutic dosage, side-effects are frequent. Treatment was begun in these patients with 2 tablets four times daily after meals and at bedtime. This dose produced a considerable amount of constipation and dryness of the mouth with blurring of vision. Reduction of the dose to 1 tablet produced the same therapeutic results, with significant lessening of side reactions.

Results:—The psychotherapeutic effect of a new medication and a new dietary regimen cannot of course be excluded and may have influenced the response at the *onset* of treatment. In view, however, of the prolonged period of study the psychological effect can be nullified.

Response was classified according to three criteria: 1. Complete relief. 2. Satisfactory relief in general but occasional pain, especially at night. (The patients in this group usually had to take an additional tablet.) 3. Transient or no relief.

Adequate relief was obtained in 97 per cent of the patients treated with tablet P and a full diet (Table I). The favorable response was in almost all cases rapid. All patients who benefited had relief within 24 to 48 hours after starting treatment, and in practically all cases were symptom-free during the period of the study. The clinical response was supported by follow-up roentgen studies.

When for one reason or another the medication was discontinued, about one-half the patients, particularly those with chronic ulcers, experienced a recurrence of their previous symptoms and it was noteworthy that use of other antiulcer preparations did not give as complete and satisfactory relief as did tablet P when it was resumed. There were no clinical recurrences as long as the patients continued on the medication, regardless of the diet employed.

The incidence of complications was extremely low in this series. No perforations occurred. Two patients had bleeding episodes during treatment, although the bleeding was minimal and in both instances was easily controlled without transfusions. There was one case of pyloric obstruction, requiring resection in a patient with a 15-year history of recurrent duodenal ulcer. In this case the ulcer was resistant to medical treatment; the operative findings indicated that no type of medical management would have been effective.

The series thus has a complication rate of less than 3 per cent, contrasting markedly with the usual rate of complications, which has been reported as high as 29 per cent.

The results in general may be best illustrated by the following typical case history reports.

Case 1:—J. M., a white male, aged 39, was first seen by me in November, 1955 because of recurrent episodes of duodenal ulcer pain with poor response

TABLE I

MEDICATION OF 145 PEPTIC ULCER PATIENTS WITH TABLET P AND UNLIMITED DIET

Results	Number of Patients	%
Complete relief	115	80
Satisfactory relief (occasional pain at night)	25	17
Transient or no relief	5	3

to diet and various antacids and other medications. He was employed in the Transit System in a position that carried considerable tension and anxiety with it. His ulcer history went back for about six years with positive x-ray findings on many occasions. Although relief of his pain was fairly constant with food, the patient had become aware recently that milk or other dairy products would not provide consistent relief, and in fact, milk would exacerbate his pain and produce nausea and vomiting. He had also experienced unpleasant side-effects such as dizziness, nausea, and headaches when taking many of the newer synthetic anticholinergics and antispasmodics.

Gastrointestinal x-ray series (Fig. 1) showed a small ulcer on the lesser curvature aspect of the duodenal bulb. General physical examination was negative. The blood count was normal and the stool was negative for occult blood. The patient was placed on an unrestricted diet except for the elimination of milk, and was given one tablet P four times daily, after each meal and at bed-

time. When seen four weeks later, he reported that he had been practically free of pain during the day but did have some moderate discomfort during the night. He was instructed to continue but was told to take two tablets upon retiring and preferably with some food. On this regimen he continued to feel quite well with no recurrence of his ulcer pains and no side-effects except for mild constipation which was easily handled with small doses of mineral oil and Milk of Magnesia. In March, 1956, he was again x-rayed (Fig. 2), and the previously demonstrated ulcer crater on the duodenal bulb was no longer present. The patient has continued on his medication and to date has been free of any symptoms.

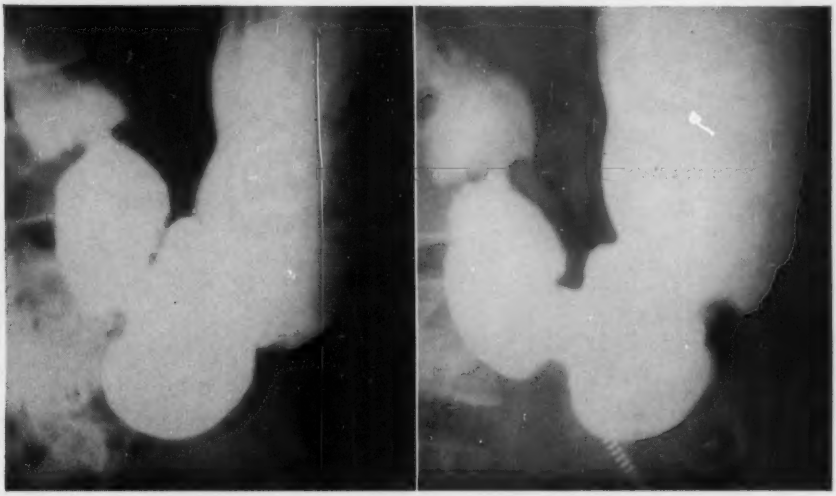

Fig. 1 Fig. 2

Fig. 1—J. M., 24 October 1955. Small duodenal ulcer on lesser curvature, before treatment.
Fig. 2—J. M., 8 March 1956. Ulcer healed, after treatment.

Comment:—This case well exemplifies the diverse and ordinarily little appreciated factors that interfere with the adequate treatment of duodenal ulcer. The realization that each recurrent ulcer attack meant a rigid restricted diet and medication always imposed a threat to this patient's job security. Inevitably he would increase his anxiety, and fail to secure relief of his pains. In addition, he developed allergic reactions to many of his medications and an intolerance or actual sensitivity to milk so that the usual dietary regimens would increase rather than decrease his pain and discomfort. His first adequate relief that persisted was then obtained from an unrestricted diet, and the elimination of milk and simple nonconfining medication that produced no reactions.

Case 2:—D. G., a 48-year old white man, was seen in August, 1955, for the relief of postprandial epigastric pains. These had been present for about eight

years, recurring twice yearly in the late winter and early fall or late summer. Relief was usually obtained with a Sippy diet and the use of various antiulcer preparations. Although medication was not maintained on a continuous basis, the patient did adhere to his diet, but despite this the attacks would recur twice yearly. There had not been any complications such as hemorrhage or obstruction. Physical examination was essentially normal. The blood count was within normal limits and the stool was negative for occult blood. Gastrointestinal x-ray series (Fig. 3) demonstrated a small ulcer crater on the lesser curvature of the parsmedial. The duodenal bulb was normal. Patient was not on any therapy, and several weeks later, a repeat gastrointestinal series (Fig. 4) again confirmed the presence of the previously described gastric ulcer. Gastroscopy was performed in September, and while the ulcer could not be visualized, the mucosa of the stomach presented a picture of hypertrophic gastritis and peristaltic ac-

Fig. 3 Fig. 4 Fig. 5

Fig. 3—D. G., 16 July 1955. Ulcer crater on lesser curvature of parsmedia, before treatment.
Fig. 4—D. G., 18 August 1955. Gastric ulcer, before treatment.
Fig. 5—D. G., 28 November 1955. Healed gastric ulcer, after treatment.

tivity appeared good. Accordingly, treatment was initiated with an unrestricted diet and tablet P four times daily, after meals and upon retiring. Patient was seen at two week intervals and reported that his pains had ceased within 24 hours of starting the medication and that he felt quite well with no epigastric discomfort whatsoever. There were no side-effects. He had mild constipation the first few days of taking the tablets, but this improved with mineral oil, which was required for the first week only.

He continued symptom-free, and in October the stomach was again x-rayed (Fig. 5) and this time the gastric ulcer was not demonstrable. A full diet and tablet P were continued, and re-examination in December, 1955, again failed to show evidence of gastric ulcer. The patient has continued to take the medication continuously, and at the time of this report, has had no recurrences of his previous ulcer pains.

Case 3:—D. H., a 24-year old white woman, was seen in March, 1955, because of persistent epigastric pains, usually occurring one or two hours after meals and relieved by food and alkalis. Her history went back for many years with a characteristic pattern of recurrences in the spring and fall. All her previous episodes, however, were mild and transient, and she never sought medical help or was x-rayed. Occasionally, the pains would be associated with nausea and vomiting. Her present episode was more severe and prolonged than usual, and there was more nausea and vomiting. Relief at this time from food and self medication was not consistent or adequate. Her general condition was good. Blood count showed a mild hypochromic anemia and the stool was negative for occult blood. Gastrointestinal x-ray series (Fig. 6) showed a duodenal ulcer.

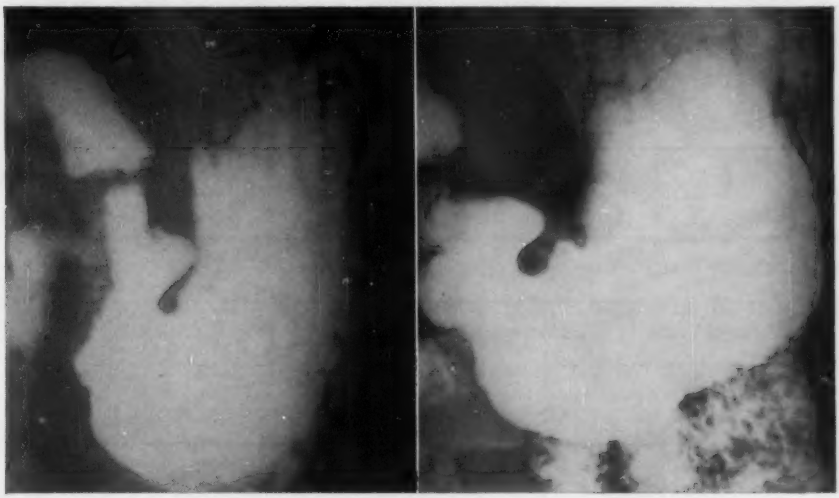

Fig. 6 Fig. 7

Fig. 6—D. H., 23 March 1955. Duodenal ulcer, no treatment.
Fig. 7—D. H., 2 November 1955. Healed duodenal ulcer, after treatment.

The patient was placed on an unrestricted diet and given tablet P, two tablets four times daily, after meals and at bedtime. She was seen again four weeks later and reported that all her symptoms had ceased within 24 hours and she felt fine, however, she had become quite constipated and complained of mild dryness of the mouth. At this time, the dosage of tablet P was reduced to one tablet at a time. She was again seen about eight weeks later and was still symptom-free and the constipation had improved markedly with the reduction to one tablet doses, so that occasional doses of mineral oil and Milk of Magnesia sufficed. Another x-ray (Fig. 7) in November, 1955, disclosed that the ulcer previously described had healed. Up to the time of this report, the patient has continued on therapy with no recurrences of her ulcer symptoms.

Side-effects were graded as "none to mild" if so slight as to be ignored by the patient; "moderate" if controlled by simple measures, without interference with the medication; and "severe" if stronger measures were required for relief (Table II).

It is to be noted that almost all patients who complained of severe side-effects still preferred to continue with the medication because of the marked relief from their ulcer symptoms and because of the psychological and therapeutic advantages of a full and unlimited diet.

The commonest and most annoying of the side-effects was constipation but this could be easily overcome and kept under control with such mild laxatives as mineral oil and Milk of Magnesia. In only a few instances was it necessary to use more drastic laxatives. Other side-effects, such as reduced salivation and

TABLE II

SIDE-EFFECTS OF MEDICATION WITH TABLET P

Side-Effects	None to Mild		Moderate		Severe	
	No. Patients	%	No. Patients	%	No. Patients	%
Constipation	87	60	41	28	17	12
Blurred Vision	139	96	5	3	1	.7
Reduced Salivation	141	97	4	3	0	—

blurring of vision were usually less frequent and usually subsided spontaneously as the patient continued with the medication. There was one case each of mild urinary obstruction, heartburn, and flatulence. None of the patients complained of dizziness, headaches and the like. In no case was it necessary to discontinue treatment because of the severity of side-effects.

SUMMARY

1. The rationale of treating peptic ulcer with antacids, and scopolamine methylnitrate or methylbromide as an anticholinergic, and Vitamin C, was proved by adequate relief of symptoms and roentgen evidence of healing in 97 per cent of 145 private patients.

2. These quaternary salts of scopolamine exert a potent and prolonged anticholinergic effect when given orally; in therapeutic doses, side-effects are minimal.

3. Addition of Vitamin C to the regimen is desirable.

4. Restricted ulcer diets probably interfere with and delay the healing of ulcers in addition to producing vitamin and protein deficiencies. Relief of symptoms and healing of peptic ulcer can be achieved on an unrestricted and unlimited diet with use of the medication described. The tremendous psychological benefit provided by allowing the patient to live and eat as a normal individual, without interference with his occupation (which would introduce an element of insecurity) is a potent force in the treatment of what probably is a basically psychosomatic disease.

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A SIMPLE METHOD FOR IMPROVING VISUALIZATION OF THE HYPERMOTILE STOMACH AND DUODENAL BULB

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Standard texts describing various methods of roentgen examination of the gastrointestinal tract emphasize the difficulties encountered in individuals with an atonic stomach plus spasm of the pylorus, in whom the barium mixture passes very slowly through the pylorus so that the duodenal bulb is poorly defined[1]. Less attention has been paid to a more frequently encountered group of patients with duodenal ulcer or other hypermotile conditions, wherein empty-

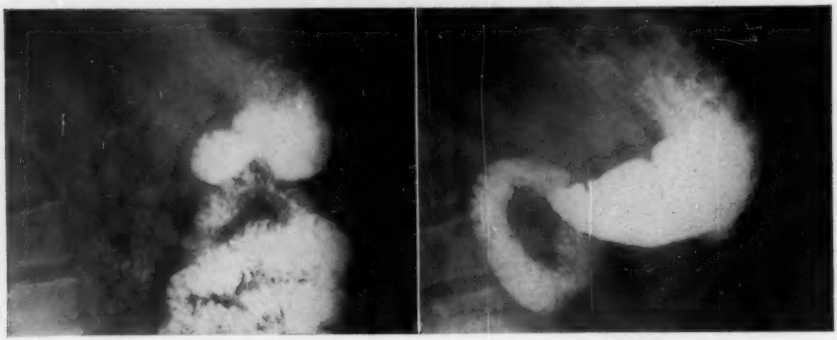

Fig. 1a

Fig. 1b

Fig. 1a—Right oblique film. Extremely rapid emptying of barium from stomach and duodenum; proper delineation not possible on repeated examination.

Fig. 1b—Right oblique film after 15 mg. of Pro-Banthine intramuscularly; stomach, duodenal bulb and duodenal curve well delineated.

ing of the stomach and duodenal bulb is so rapid that accurate roentgen visualization becomes extremely difficult and requires repeated and laborious manipulations to determine the presence or absence of underlying pathology.

There is no "average" emptying time of the human stomach. The time varies with age, sex, type of stomach (habitus) and with the type of meal employed. It is also true that the more a patient is starved, the faster the initial emptying of the stomach will take place[2]. Buckstein[3] notes that abnormally rapid emptying

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of the stomach may occur as a result of exaggerated peristaltic activity, or in the presence of a gaping pylorus, particularly due to rigid infiltration. He also emphasizes the importance of the effect of the emotions upon the emptying time of the stomach. It is not at all uncommon to examine a patient for the first time and find apparent evidence of functional derangement of tone, peristalsis and motor function. The anxiety of the patient and the strangeness of his surroundings may contribute to this change. Reexamination at a later date, when the patient's fears have been allayed and he is less apprehensive, may show the motor manifestations to be more normal. This, however, involves several examinations, delays making an accurate diagnosis, and increases the cost. A

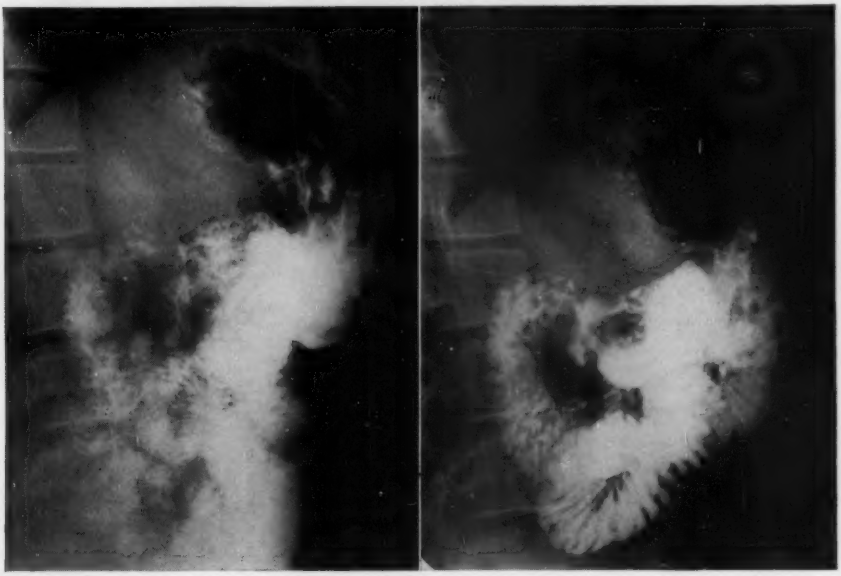

Fig. 2a Fig. 2b

Fig. 2a—Basic film, duodenal irritability and rapid emptying.
Fig. 2b—After 30 mg. of Pro-Banthine by mouth. Ulcer deformity and delay in motility.

method of examination which is simple and which can obviate the difficulties resulting from such hypermotility at the first visit to the office or clinic is the subject of our presentation.

The problem of gastric atony can be readily overcome by the use of physostigmine 1/25 gr. by mouth, or 1/50 gr. subcutaneously as outlined by Ritvo and Weiss[4]. In their patients the duodenal bulb could not be properly visualized because pyloric spasm prevented the barium from entering the duodenum. Injections of morphine or of insulin have also been utilized to increase tone and produce vigorous contractions of the stomach in an effort to overcome such

pyloric spasm[5,6]. These measures have obvious disadvantages when used in office or clinic practice.

Myerson and Ritvo found benzedrine to be very effective in abolishing spasm of the gastrointestinal tract. This drug is sympathomimetic in character and its administration is followed by a relaxation of spasm of the stomach, pylorus and intestines. They state that more accurate study of the stomach and duodenum is possible after the disappearance of the spasticity as the stomach empties more readily; and small ulcer craters, especially about the pylorus and duodenum are much more clearly visualized[1,7].

Fig. 2c—After 15 mg. of Pro-Banthine intramuscularly. Deformity and delay in motility more definite.

The patients who created the basis for our investigations, however, presented an entirely different problem. They were all individuals in whom there was evidence of an unusual hypertonicity of the stomach associated with extremely rapid emptying through the pylorus. In each instance the flow of barium was so rapid that neither the stomach nor the duodenal bulb could be adequately studied. This is especially true of patients with the hypersthenic habitus and high transverse stomach[8].

This problem has disturbed roentgenologists and gastroenterologists for a long time and up to a few years ago some success in controlling this hypermotility was achieved by the use of atropine or atropine-like drugs. Unfortu-

nately, effective doses of atropine usually created undesirable side-effects. It was not until the advent of Banthine, Pro-Banthine, and similarly potent anticholinergic drugs that more effective control of this hypermotile state is now becoming a reality.

Roback and Beal[9] and Schwartz et al[10] demonstrated that 30-40 mg. of Pro-Banthine by mouth or 10-20 mg. by intramuscular injection resulted in marked and prolonged inhibition of gastrointestinal motility. Our experiences with Pro-Banthine[11] in the treatment of duodenal ulcer and other diseases with hypermotile manifestations afforded us an excellent opportunity to study the value of this drug in improving the x-ray visualization of the hypermotile stomach and duodenal bulb. This report is based on such a study in 97 patients who presented themselves with this diagnostic problem during the past three

Fig. 3a—Film without Pro-Banthine. Gastric carcinoma suspected but not visualized.

years. The use of Pro-Banthine is simple, rapid, and almost dramatic in its efficacy. It also may serve the double purpose of relieving the pain of a patient with active ulcer while the roentgen examination is being performed.

Method

The examination is performed as usual, after a fast of 12 hours. If previous experience with the patient has indicated a state of hypermotility, an injection of Pro-Banthine is given intramuscularly ten minutes before the barium is ingested. If the hypermotility reveals itself without warning after the first swallow of barium, our procedure is modified. Usually sufficient barium remains in the stomach to demonstrate the mucosal pattern so that compression studies and spot films can be made. The patient is then given an injection of 10 to 20 mg. Pro-Banthine intramuscularly, the dose varying with the weight of the patient and the degree of the rapidity of emptying. Ten minutes after the injection

another glass of barium mixture is given and a complete delineation of the stomach and duodenal bulb is easily and unhurriedly obtained. More accurate study of the stomach and duodenum is possible after the disappearance of the hypermotile state, and frequently small ulcer craters not previously visualized may fill and be well delineated. An excellent small bowel pattern is also easily obtained by hourly studies. While it is true that the delay in motility following the injection of Pro-Banthine is unphysiologic, the resultant excellent delineation of stomach, duodenum and small bowel will more than compensate for the inability to measure normal motor activity of the gastrointestinal tract. If an

Fig. 3b—Five-minute film after 15 mg. of Pro-Banthine intramuscularly. Carcinoma outlined.

intramuscular injection is not feasible, the same effect can be obtained by giving 30 mg. of Pro-Banthine by mouth with a minimal swallow of water 20 minutes before the x-ray examination begins. The intramuscular injection is of course, more effective because of the rapidity of action and the certainty that the full dose has been absorbed. If the patient is warned about the mild drying effect in the mouth, no other untoward effects need be anticipated.

Pro-Banthine is contraindicated in the presence of glaucoma since mydriasis, if it occurs as a side-effect of therapy, is undesirable. In patients with pro-

static hypertrophy and urinary obstruction, varying degrees of urinary difficulty may be observed following Pro-Banthine administration due to its inhibitory effect on the bladder musculature. Such patients should be observed closely until they have gained some experience with the drug. Urinary difficulty often may be avoided by advising micturition at the time of taking medication. Pro-Banthine should be used with caution, if at all, when a chronic, stenosing, duodenal or pyloric ulcer or other obstruction of the gastrointestinal tract is present or suspected, because the inhibition of gastrointestinal motility effected by the drug may interfere with the passage of gastrointestinal contents past the site of obstruction[11].

The following case reports will help to demonstrate the difficulties encountered in routine gastrointestinal investigations, both of normal patients and in those with organic diseases, which could not be properly diagnosed until the

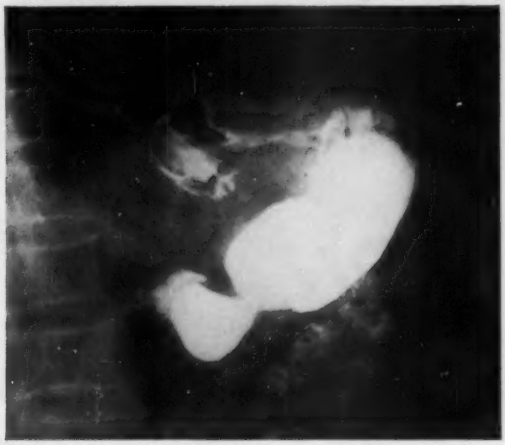

Fig. 3c—Fifteen-minute film after Pro-Banthine intramuscularly. Carcinoma delineated.

hypermotile manifestations were controlled by the administration of Pro-Banthine.

Case Reports

Case 1. Visualization of normal stomach and bulb:—B. B., male, age 52 with typical hypersthenic habitus, complained of vague epigastric distress of several years' duration when first seen. Roentgenologic examination of the gastrointestinal tract on several occasions persistently revealed an extremely rapid emptying of barium from the stomach with rapid passage through the duodenum. The duodenal bulb was apparently markedly irritable and consequently was not visualized clearly on any of the roentgenograms (Fig. 1a). Following the injection of 15 mg. of Pro-Banthine intramuscularly, rentgenograms showed the stomach to be completely normal. The duodenal bulb was clearly outlined

and the entire duodenal sweep was seen for the first time (Fig. 1b). A diagnosis of "chronic anxiety state" was made and finally established by subsequent examinations.

Case 2. Visualization of abnormal duodenal bulb:—J. K., male, age 28, presented a history of epigastric pain for several years. Roentgenologic examination at the first visit revealed a markedly irritable duodenal bulb with extremely rapid emptying of the barium from the stomach and duodenum. It was impossible to delineate a lesion clearly although ulcer was suspected clinically (Fig. 2a). He was given 30 mg. of Pro-Banthine by mouth and roentgenography was repeated. There was a substantial delay in the emptying of barium from the stomach and duodenum. At this time an ulcer deformity was visualized (Fig. 2b). Still better visualization was attempted by administering 15 mg.

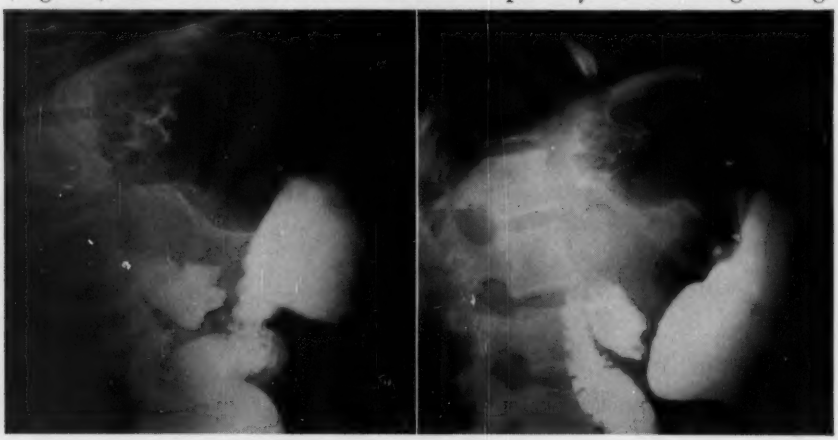

Fig. 4a Fig. 4b

Fig. 4a—Basic film. Pronounced hypermotility of stomach and bulb; diagnosis not possible.
Fig. 4b—Five-minute film after 15 mg. of Pro-Banthine intramuscularly. Large gastric ulcer on lesser curvature clearly visualized.

of Pro-Banthine intramuscularly. Five minutes after the injection the deformity was even more clearly outlined (Fig. 2c). This patient was operated upon and a duodenal ulcer penetrating posteriorly into the pancreas was found.

Case 3. Visualization of gastric carcinoma:—A. G., male, age 68, presented himself with complaints of mild dysphagia, anorexia, moderate weight loss and epigastric pain. Roentgenologic examination of the gastrointestinal tract revealed a peculiar pouch-like projection on the lesser curvature of the cardiac end of the stomach (Fig. 3a). A diverticulum or neoplastic lesion was suspected, but visualization was not sufficiently clear to permit a diagnosis. The roentgenologic examination was repeated and again failed to outline the lesion clearly. Therefore the patient was given 15 mg. of Pro-Banthine intramuscularly

and roentgenograms were again obtained. Sufficient barium was retained in the cardiac end of the stomach so that the lesion was finally outlined. A tentative diagnosis of carcinoma of the cardiac end of the stomach, probably extending into the lower portion of the esophagus, was made. The patient subsequently was operated upon and the diagnosis corroborated (Figs. 3b and 3c).

Case 4. Visualization of gastric ulcer:—J. R., male, age 50, when first seen complained of severe abdominal pain for six weeks. The first gastrointestinal examination of the patient revealed marked hypermotility of the stomach and bulb, and it was not possible to visualize a lesion (Fig. 4a). The patient's symptoms, however, were so suggestive of an ulcer that he was re-examined after the injection of 15 mg. of Pro-Banthine intramuscularly. There occurred a marked diminution in motility and a huge gastric ulcer was easily visible on the lesser

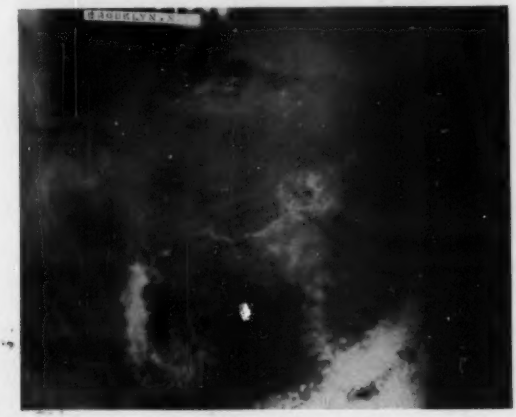

Fig. 5a—Unusual hypermotility of stomach and duodenal bulb. Complete emptying of barium from stomach within five minutes.

curvature at the junction of the upper and middle thirds of the stomach (Fig. 4b). This is an excellent example of delineation of a lesion which had escaped detection with the ordinary technic of gastrointestinal roentgenography.

Case 5. Duodenal ulcer penetrating into pancreas misdiagnosed as "irritable" bulb and psychoneurosis:—J. D., male, age 30, had been complaining of abdominal pain for nine years. Several roentgen examinations while in the Army resulted in a diagnosis of "irritable" bulb and psychoneurosis, and the patient was discharged as a psychoneurotic. His complaints, however, continued and further gastrointestinal investigations at the Veterans Hospital on several occasions did not reveal any change in the diagnosis. He presented himself at the office of the senior author with complaints of severe abdominal pain radiating into the back and intractable in nature. Our first roentgenological examination revealed a most unusual hypermotility of stomach and bulb with com-

plete emptying of the glassful of barium from the stomach within five minutes after its ingestion (Fig. 5a). A repeat examination a week later was similarly unrevealing (Fig. 5b). The patient then was given 20 mg. of Pro-Banthine by intramuscular injection and 10 minutes later another glass of barium. An excellent delineation of both stomach and duodenal bulb was obtained. For the first time a markedly deformed bulb with a crater penetrating posteriorly into the pancreas was clearly outlined (Fig. 5c). After several weeks of medical therapy his symptoms continued unabated and the patient was advised to return to the local Veterans Hospital for surgery. In spite of his detailed description of our x-ray findings, their routine roentgenological examination again re-

Fig. 5b—Repeat examination one week later, similarly unrevealing.

revealed only an "irritable" bulb. It was finally necessary for us to send our films to the hospital for their perusal before they would agree to the diagnosis and surgical intervention. Operation confirmed our diagnosis. This and several other similar cases which we have studied have indicated that many patients are frequently falsely labeled as "psychoneurotic" because the diagnosis is obscured as a result of the hypermotility of stomach and bulb. Every patient in whom there is failure of proper visualization of the stomach, duodenum and small bowel, as a result of such hypermotility, certainly deserves the simple re-evaluation with Pro-Banthine to clarify diagnosis.

Case 6. Visualization of huge postbulbar ulceration:—J. C., male, age 32, had extremely severe epigastric pain of two years' duration with radiation to the back. Several gastrointestinal studies had been performed elsewhere but no

Fig. 5c—After 20 mg. Pro-Banthine intramuscularly. Excellent delineation of stomach and markedly deformed bulb.

ulcer was found. Roentgenologic examination at this time revealed a duodenal deformity, marked irritability of the duodenal bulb and a suggestion of irritability of the descending duodenum (Fig. 6a). The latter, however, could not be better delineated when roentgenography was repeated (Fig. 6b). After 15 mg.

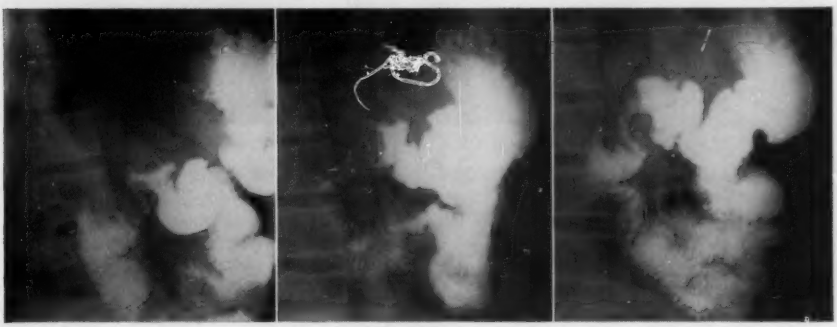

Fig. 6a Fig. 6b Fig. 6c

Fig. 6a—Basic film. Duodenal deformity and irritability.
Fig. 6b—Repeat film. Duodenal deformity and irritability.
Fig. 6c—After 15 mg. of Pro-Banthine intramuscularly. The huge irregular duodenal bulb and extent of postbulbar ulceration first appreciated.

of Pro-Banthine intramuscularly another examination for the first time revealed a huge irregular duodenal bulb with ulceration extending into and involving at least one inch of the descending duodenum. The patient was maintained

comfortably on 30 mg. of Pro-Banthine three times a day with 45 mg. at night, but surgery was recommended following an episode of melena. The presence of the above described ulceration with penetration into the pancreas was confirmed at the operation (Fig. 6c).

Case 7. Visualization of an ulcer, hidden by a congenital duodenal redundancy:—L. B., a news photographer was seen with complaints of abdominal pain of several years' duration. Clinically the symptoms were those typical of a peptic ulcer, but several gastrointestinal investigations at other institutions and also at the office of the senior author failed to reveal a lesion. Our examination

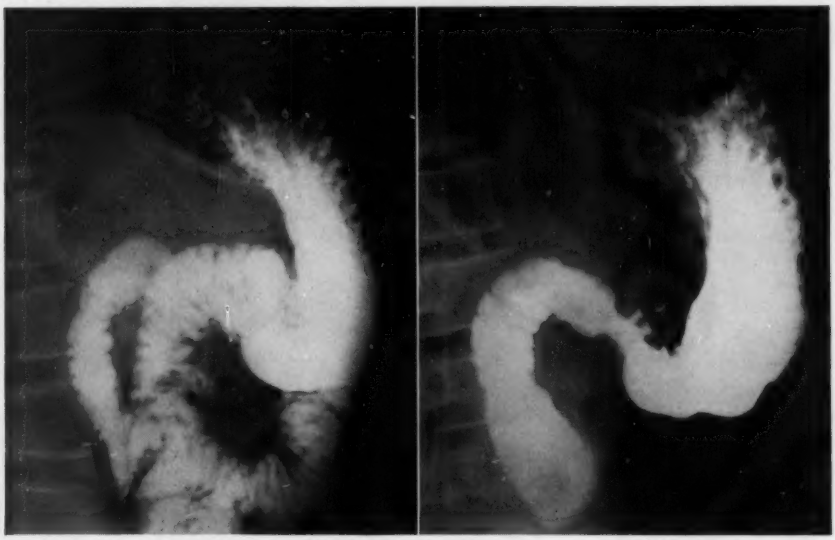

Fig. 7a Fig. 7b

Fig. 7a—Duodenal bulb constantly obscured by congenital figure 8 duodenal loop.
Fig. 7b—After 15 mg. Pro-Banthine intramuscularly, motility effectively delayed. Clinically diagnosed ulcer easily visible.

revealed a hypermotility of stomach and duodenum with a congenital figure ∞ configuration of the duodenum which, because of the duodenal redundancy, prevented proper visualization of the antrum and bulb (Fig. 7a). Repeated routine examinations again were of no avail. Another examination after 15 mg. of Pro-Banthine intramuscularly effectively delayed the motility so that the clinically diagnosed ulcer was easily visible (Fig. 7b).

Comment

The preceding cases are merely a few examples of the many we have encountered during the past three years in which a diagnosis of an organic

lesion was either clouded or made difficult by the hypermotile activity of the stomach and duodenal bulb. In many instances the roentgenological diagnosis of an "irritable" stomach and bulb has caused much suffering because of the tag of "psychoneurosis" which often accompanies such a diagnosis. We hope that the diagnosis of "irritable" bulb will be less frequently made when the simple procedure such as we have outlined is performed. By utilizing the anticholinergic drugs the hyperactivity of the stomach and bulb can be brought under control. Thus, underlying pathology, if present, can be leisurely and more carefully studied.

Summary and Conclusions

Anticholinergic drugs are an important new aid in the roentgenographic visualization of the gastrointestinal tract. They may be given orally (30 mg.) or preferably intramuscularly (10-20 mg.) prior to ingestion of the barium.

By inhibiting motility an anticholinergic drug such as Pro-Banthine aids in delineating more clearly the normal gastrointestinal tract and also enables better visualization of lesions of the gastrointestinal tract, sometimes making it possible to demonstrate a lesion that would otherwise be undetectable.

By utilizing this procedure the diagnosis of "irritable" bulb should be less frequently required.

Illustrative cases have been presented to demonstrate its usefulness in clarifying the diagnosis in doubtful cases with hypermotile manifestations.

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THE TIMED INTEGRATION OF STOOL HYDRATION AND PERISTALTIC STIMULATION IN CONSTIPATION CORRECTION*

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In spite of the well established clinical findings[1,5] that constipation is primarily due to a neuroperistaltic deficit, recent attention has been directed toward the consistency of the fecal mass[6,12]. A review of the clinical literature on stool softeners reveals the almost unanimous viewpoint that stool softeners are not intended to replace or substitute for the neurotropic constipation correctives and that peristaltic stimulants should be administered with the surface active agents for optimal response. The statement of Wilson and Dickinson[6], the originators of the concept of stool-softening, that "the use of dioctyl sodium sulfosuccinate by itself should not be considered a satisfactory method of management" for dysfunction of part of Auerbach's plexus (in reference to the treatment of megacolon), is restated by the most recent investigators[11] who note that DSS, "appears to be without laxative action" and that, "where inadequate peristalsis is a primary factor, additional laxation may be necessary." In view of this widely concurred-in opinion, it was believed to be important to explore the combined use of neuroperistaltic stimulants with surface active agents.

While ample evidence of the surface activity of stool softeners exists, data describing the temporal pharmacodynamics of stool hydration is lacking in the literature. The questions of, how long does it take to convert a concrete fecal mass into a soft stool, and, what concentrations of surface active materials are required to bring this change about, still remain to be answered. Data describing the interval following oral administration and accumulation of optimal concentration of surface active materials at the fecal mass, is also significant in view of the coordinated activity required, but is notably absent.

This study is concerned with these interrelated aspects of the mechanics of stool-softening combined with peristaltic stimulation so as to establish the proper conditions for safely and rationally meeting this challenge of timed integrated activity in clinical constipation correction.

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The materials used in this study were supplied by the Medical Department of The Purdue Frederick Company, New York City.

Methods and Materials

Dioctyl sodium sulfosuccinate, U.S.P., (DSS) is the surface active agent which has received the widest attention and clinical study as a stool-softener. It has been accepted[12] for this purpose by the Council on Chemistry and Pharmacy of the American Medical Association and was selected for this study because of its well defined and accepted properties.

DSS has been recommended for clinical use over a wide dosage schedule intended to deliver quantities of the agent to the fecal mass ranging from 0.01 per cent to 1.0 per cent or a hundred-fold variation[13]. These levels have been derived from an empiric analysis based upon a calculated fecal mass of 200 gm. for the "average normal" adult[14]. The minimal concentration of 0.01 per cent would, therefore, be supplied by 20 mg. of the compound. While it is recognized

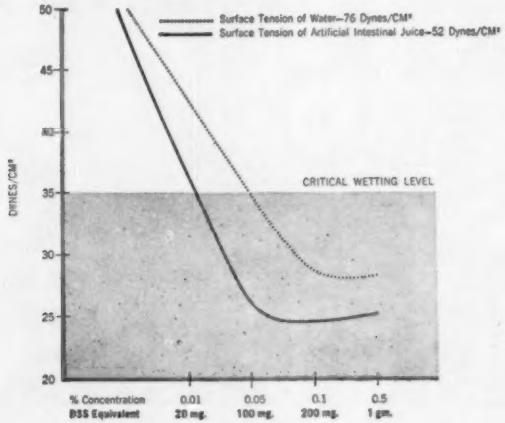

Fig. 1

that this dose range is extremely flexible, it was used as a guide for evaluating the relationship between time of contact and surface activity in this study.

The surface tension of a graded series of dilutions of DSS, corresponding to the clinically recommended dosage range was determined, utilizing both water and artificial intestinal juice[15] as the diluent (Fig. 1). In considering the surface tension lowering capacity of the DSS, utilization of the literature values for distilled water is undoubtedly misleading. The intestinal fluid contains surface active agents (taurocholic acid salts), as well as inorganic salts, which have a profound potentiating effect on DSS.

It is accepted that the surface tension should be below 35 dynes per cm., when rapid wetting is desired[16]. Simple inspection of the concentration-gradient curves (Fig. 1) reveals that this criteria is met by minimal dosage and the

median optimal dose-response relationship within this range of 0.015 to 0.050 per cent (from 30 to 100 mg.) is 50 mg. of DSS.

The critical wetting range is achieved by 30 mg. of DSS and the curve levels off at 100 mg. concentration. There is no significant advantage either theoretically or clinically to using larger amounts of the surface active agent if surface activity is the basis for stool-softening. The median value of 50 mg. produces a surface tension of 30.4 dynes while the plateau of the curve is reached at 26.1 dynes with 100 mg. The 100 per cent increase in dosage, therefore, produces a decrease of only four dynes in the surface tension. This difference could not be distinguished clinically, and the use of quantities of surfactant in excess of this effective range is of no advantage.

Fresh samples of "dry", hard, fecal material were incubated with varying concentrations of DSS-Artificial Intestinal Juice under static conditions dupli-

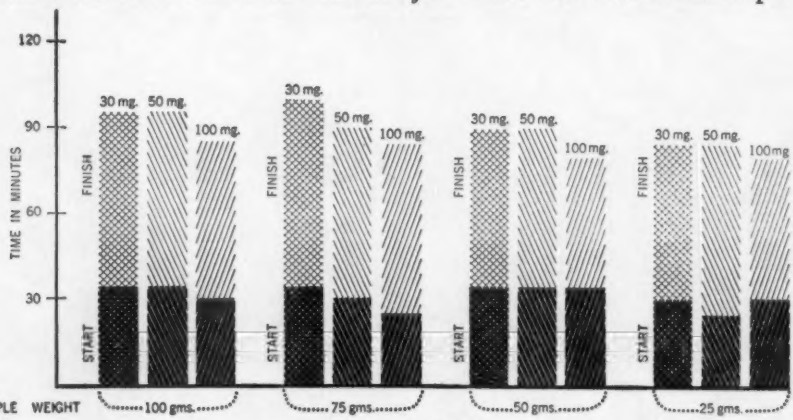

Fig. 2—The stool-softening behavior of DSS.

cating colonic immotility. The time of contact necessary to cause the first signs of physical change (swelling, fracturing, etc.), and that required for disorganization (or disintegration), were recorded, (Table I and Fig. 2). The values observed are in good agreement with the activity described in the surface tension-concentration curves, and there appears to be little advantage in using quantities in excess of 50-100 mg. of DSS in order to effect penetration of fluid into the fecal mass. It is of interest to note that weight of material was not significant and the smaller fecal masses required just as long a period of contact with the stool-softener as did greater quantities. Thus, the pediatric stool concretion requires the same surface wetting capacities as does the greater mass of the geriatric patient.

The interval between the administration of a dose of stool softener and its concentration at the fecal mass was studied with the aid of three colostomy

patients. These patients, with well-functioning colostomies, were free of any active gastrointestinal disease and in good general health. Two of the colostomies were created approximately 15 months earlier, as a consequence of a resection for rectal carcinoma, while the third was a transverse colostomy after a resection for ulcerative colitis, three years previously.

By feeding these patients known concentrations of stool softener, and determining the time required for it to reach the colon, (as evidenced by surface tension depression), an approximation of the "lag-period", following ingestion would be obtained. It is recognized that an individual with a completely functioning gastrointestinal tract may present quantitatively different data than that of a colostomy patient, but the reproducible approximations derived are significant because of the trends indicated. This is more readily appreciated when we

TABLE I

EFFECT OF SURFACE TENSION ON STOOL HYDRATION

Weight Grams (a)	Surface of Solid in Area (b)	35 Dynes (30 mg.) (c)		30 Dynes (50 mg.) (c)		26 Dynes (100 mg.) (c)	
		Start (d)	Finish (e)	Start (d)	Finish (e)	Start (d)	Finish (e)
100	54 cm.^{2}	35 min.	95 min.	35 min.	95 min.	30 min.	85 min.
75	48 cm.^{2}	35 min.	100 min.	30 min.	90 min.	25 min.	85 min.
50	40 cm.^{2}	35 min.	90 min.	35 min.	90 min.	35 min.	80 min.
25	32 cm.^{2}	30 min.	85 min.	25 min.	85 min.	30 min.	80 min.

(a) Approximate weight of solid plus 2 gm. (b) Approximate surface area calculated from general formula for cylinder area. (c) Refers to surface tension of test solution and the mg. equivalent of DSS to produce this. (d) The first signs of physical change. (e) Disorganization or disintegration. (f) Recorded to nearest five-minute period.

consider that the "lag-period" involves passage through the upper gastrointestinal tract and the small intestines where the stool is not formed. Since stool-softening occurs only in the colon, the use of this technic should afford information describing the interval for the DSS to reach the descending colon and the transverse colon, where the effective action is carried out.

Samples of the colostomy exudate were obtained throughout the day, then clarified by centrifugation and the surface tension determined. These values served as a base-line control. The samples were obtained in the morning upon arising (prior to breakfast), and were generally concluded just prior to dinner. The food intake during this test period was limited, with fats excluded, in order

to minimize the activity of the bile salts which are known to be potent surface active agents. The diet was standardized during the entire test interval for the group.

Varying concentrations of DSS were fed these patients and samples of exudate collected at intervals and the surface tension determined. The test days were alternated to permit a rest period between doses. The desired amount of

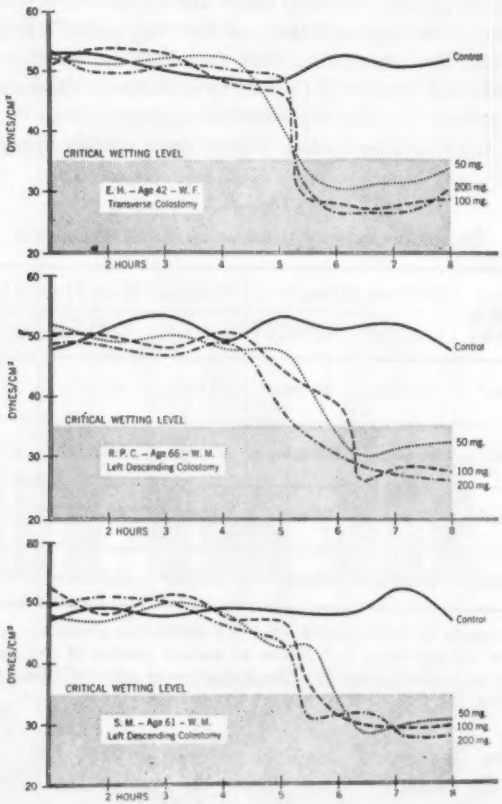

Fig. 3—Surface tension of exudate after DSS.

DSS was administered as a capsule with four ounces of water as a single dose. A drop below the base-line control surface-tension previously determined, signified the advent of the stool softener and a depression of the surface tension below 35 dynes/cm. was considered to be a clinically effective concentration. By correlating the surface tension measurement with time, an indication of the time lag due to passage through the gastrointestinal tract, is obtained (Fig. 3).

The timing index of the mechanics of stool softening is expressed by the sum of the intervals of the passage through the gastrointestinal tract and that required to effect disorganization of the fecal mass. Because of the variables involved, this is best described as a range rather than a fixed value (Table II), which rather pointedly demonstrates the similarity of affect within the critical range and the futility of using quantities in excess of this range.

The criteria for selecting the proper neurotropic stimulant to be used in conjunction with the surface active agent is, in part, determined by the data on the mechanics of stool-softening. The peristaltic stimulant must be specific for Auerbach's plexus; exert its action solely in the colon; be standardized to a very high degree in order to cause a reproducible effect; produce a stimulation of the colon starting at least eight hours after ingestion and reaching its peak

TABLE II

TIMING INDEX OF STOOL SOFTENING

	Quantity of DSS		
	30 mg.	50 mg.	100 mg.
		Range in Minutes	
Initial wetting (A)	30-35	25-35	25-35
Complete wetting (B)	85-100	85-95	80-85
Passage through GI tract (c)	—	360-390	360-390
Timing Index		*Range in Hours*	
Start (A+C)	—	6.5-7.0	6.5-7.0
Complete (B+C)	—	7.5-8.0	7.5-8.0

within ten hours; cause no griping, irritation or rebound constipation and be compatible with the surfactant both chemically and physiologically. A comparison of the known properties of the commonly available constipation correctives as satisfying these criteria is presented in Table III. It appears that the standardized glycosides of *cassia acutifolia* (Senokot) most closely approximates the ideal requirements of the peristaltic stimulant to be used in conjunction with surface tension depressants and, accordingly, was combined with it in capsule dose-form.

The most successful clinical approach to constipation correction is that mediated through stimulation of Auerbach's plexus and in this regard the standardized glycosides of senna pods (Senokot) have been established as being superior[1-5,17,18,19]. The literature[17,18,19] indicates that the onset of action of Senokot is independent of the dose and that evacuation occurs eight to ten hours after ingestion with both minimal as well as maximal dosage. In order to

provide a flexibility of dosage regimen, since all individuals differ in their therapeutic needs, the median optimal effective dose of DSS (50 mg.) was combined with the minimal effective dose of Senokot (225 mg.) in each capsule. By prescribing either one or two capsules, according to the individual needs of the patient, the clinician is afforded a means of conveniently administering the therapeutic agents at optimal concentrations.

TABLE III

COMPARISON OF BEHAVIOR OF ACTIVITY OF CONVENTIONAL LAXATIVES WITH CRITERIA FOR COMBINATION WITH DSS

	Magnesium Salts (a)	Phenol-phthalein	Cascara Products	Senna-sides (Senokot)	Mineral Oil
Specific for Auerbach's plexus	No	No	No	Yes	No
Standardization	Yes	Yes	In part (b)	Yes	Yes
Action solely in colon	No	No	No	Yes	No
Action starts after six hours	No	No	In part (c)	Yes	No
Peak activity after eight hours	No	No	In part (c)	Yes	No
Irritation to GI tract	Yes	Yes	Yes	No	No
Rebound constipation	Yes	Yes	Yes	No	Yes
Normalizes stool consistency	No	No	(d)	Yes	No
Chemically compatible	No	Yes	Yes	Yes	Yes
Contraindicated in pregnancy or in nursing mothers	—	Yes	Yes	No	No

(a) Includes magnesium citrate, epsom salts and Milk of Magnesia.
(b) Some cascara products are reportedly standardized.
(c) Some investigators report "peak" activity after eight hours with initial activity earlier.
(d) No data available.

CLINICAL CONFIRMATION

The concepts of timed-integration of combined stool-softening-constipation correction were clinically evaluated in 50 patients with a history of constipation or presenting proctologic disorders, wherein daily evacuation of a soft stool was essential. The constipated patients were carefully selected and were presently

utilizing commercially available stool-softeners. These patients all had common experience of lack of predictable action, with defecation occurring on the average of two to three times weekly in spite of elevated dosage of stool-softeners being administered. These patients were considered to have a deficit of neuronal

TABLE IV

CLINICAL STUDY OF TIMED INTEGRATION CONCEPT OF SENOKAP

Indication	No. of Patients	Average Time for Evacuation after Administration			Comments
		After Previous Medication	After Therapy With Senokap		
			1st week	3rd week	
Refractory constipation (a)	32	3 times weekly-18 2 times weekly-14	10-12 hours-25 12-14 hours-1 14-16 hours-2 24 hours-4	10-12 hours-27 12-14 hours-3 14-16 hours-2	Many patients received as much as 240 mg. of DSS previously, thereby establishing that peristaltic deficit was the essential problem.
Hemorrhoids & constipation (b)	6	3 times weekly-4 4 to 5 days-2	10-12 hours-5 12-14 hours-1	10-12 hours-6	Ambulatory patients—nonsurgical series. Less trauma was experienced with diminished pain.
Posthemorrhoidectomy (c)	8	(c)	10-12 hours-6 16 hours-2	10-12 hours-8	Excellent postoperative course. Convalescence uneventful.
Postfissurrectomy (c)	4	(c)	10-12 hours-4	10-12 hours-4	Convalescence uneventful.

(a) Patients were receiving daily administration of stool-softener alone. Various commercial preparations were used, all containing DSS as an active ingredient.

(b) Some patients were taking laxatives on a relatively infrequent basis.

(c) Senokap was started 3 to 4 days postoperatively. For the most part, the patients had a history of tending toward constipation, with a predominance of hard, dry stools. There was no data available in connection with previous response to laxatives.

activity of Auerbach's plexus and, consequently, stool-softening alone was only a partial answer to their problem. A combined stool-softener and sennaside preparation (Senokap) was prescribed in a regimen of two capsules, at bedtime, reducing the dosage after two weeks, or when indicated, to one capsule at night.

The group requiring stool hydration in addition to stimulation of Auerbach's plexus, consisted of postoperative patients with drug-induced constipation, as well as those with anorectal disease. The dosage administered was two capsules at bedtime to start and diminishing to one capsule, when indicated.

The previous medication of the patients was stopped at least 48 hours prior to the administration of the test agent, and the time interval required to produce defecation after ingestion of a dose of test medication was recorded. The time-intervals were averaged for each patient on a weekly basis and the range of response determined. Because the purpose of this study was limited to the mechanics of constipation, extended clinical trials were not carried out at this time.

The subjective patient response to the medication was especially observed for undesirable side-effects.

Each patient served as their own control since their previous response to stool softeners was known. Furthermore, the ultimate laxative activity is measurable and is, therefore, capable of acting as an objective means of evaluating the results. The results of the clinical study are described in Table IV.

Results

Of the entire experimental series, 40 patients (or 80 per cent) experienced evacuation within 10 to 12 hours after drug administration; 6 (or 12 per cent) required 12 to 16 hours and 4 (or 8 per cent) required 16 to 24 hours. After two weeks of therapy, the number responding to medication within 10 to 12 hours increased from 80 to 94 per cent and only 2 patients required more than 14 hours for defecation. In none of the patients studied was the time-interval less than 10 hours for the response to be observed.

There were no side-effects observed during the administration of the drug and the patients frequently commented on the sense of well-being accompanying the return of physiologic bowel function. The contrast between the activity of the earlier use of the stool-softener alone and, that, when combined with a peristaltic stimulant was dramatic, as well as most gratifying to the patient.

Attempts at correlating the over-all effect of the lack of trauma, because of the soft stool, on the rate of wound healing were inconclusive, because of the limited number of cases. It is our impression, however, that normal bowel function together with a nontraumatic stool, is a factor in facilitating proctologic wound healing. The patients taking Senokap had an uneventful convalescence and appeared to respond better than patients on conventional cathartics. Definitive data in this connection would be available only after prolonged comparative study which was beyond the scope of the present one.

Our clinical experiences confirm the experimental findings on the behavior of the surface active agents as stool softeners and their consequent role in constipation correction. From the surface tension curves for these agents, it is evident that once the critical wetting range is achieved, the increase in quantity of agent produces only small changes in over-all effect.

The failure of the surface active agents to produce a laxative effect is not due to insufficient concentration, but is inherent in its inability to stimulate Auerbach's plexus as was established by the predictable response observed in the patients previously refractory to stool softeners alone. In view of this finding, the present trend toward larger dosage of the stool-softener seems futile. On the basis of the integrated timing required, there is no obvious difference between the 50 mg. dose and the 100 mg. dose.

Summary and Conclusions

1. The pharmacodynamics of dioctyl sodium sulfosuccinate (DSS), was investigated in connection with the mechanics of stool softening, in both *in vitro* and *in vivo* studies.

2. It was established from surface tension lowering curves that the optimal median dose of DSS for stool softening was 50 mg. There is no advantage either clinically or theoretically in utilizing amounts of the surface active agent greater than that required to produce the lowest depression of the surface tension of the system.

3. The timing of stool-softening activity is extremely important when these agents are used in combination with a peristaltic stimulant. It requires approximately 6 to 8 hours for effective stool softening following administration, and the choice of peristaltic stimulant must be determined by the timing of onset of peak activity.

4. Senokap, the combination of the surfactant (DSS), with a peristaltic stimulant of proved clinical superiority (Senokot), results in a refinement of the mechanics of constipation correction which most adequately meets the theoretical criteria for this purpose. This agent adds a new dimension to laxative therapy by integrating timed stool-softening with predictable evacuation.

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CLINICAL OBSERVATIONS WITH CANTIL, A NEW ANTICHOLINERGIC FOR COLON DISORDERS*

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Disturbed colonic motility, manifested primarily by hyperirritability and spasm, is a common cause of the abdominal distress encountered in practice. The motor-suppressive action of the newer synthetic anticholinergics might be expected to contribute significantly to the re-establishment of neuromuscular balance in disorders of the colon. The widespread activity of many of these agents, however, particularly in the upper gastrointestinal tract, often limits their clinical value. With some, the dosage required to curb colonic hyperfunction is sufficient to interfere with autonomic regulation of the bladder and other organs not involved in the disturbance presented for treatment.

In view of the frequent shortcomings of antispasmodic agents available for treatment of colonic hypermotility and spasm, we were particularly interested in the properties of the new piperidol anticholinergic agent, N-methyl-3-piperidyl-diphenyl-glycolate methobromide (Cantil)‡, reported by Biel, et al[1]. The pharmacologic studies of Long and Keasling[2] showed this postganglionic parasympathetic inhibitor to be approximately as active as atropine. It is, however, more active in inhibiting motility of intestinal preparations than in inhibiting acetylcholine depressor responses, pilocarpine-induced salivation or B-methacholine-induced lacrimation[2]. In trained unanesthetized dogs, small doses intravenously inhibited colon motility more than stomach motility in most tests[3]. Other pharmacologic studies showed that Cantil had more relaxant effect on the colon than the ileum[4] and a markedly greater effect on the colon than the bladder[5]. Because of the clinician's need for an agent that could restore normal tone and motility to the colon while exerting little or no clinically significant effects elsewhere, this selectivity for the colon was thought to be a highly desirable attribute in an anticholinergic drug. Clinical studies with Cantil were therefore undertaken in patients with functional and organic colon disorders.

Clinical Studies

Necheles et al[3] reported good to excellent results without side reactions in 17 out of 18 patients treated with Cantil for spastic colon. Kleckner has indi-

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cated that Cantil is the most effective available colonic anticholinergic drug for the dramatic remissions it has produced in steatorrhea due to massive intestinal resection or hypermotility[6] and also for its unusually effective control of obstinate diarrhea of varied origin[7].

The 79 patients comprising our series were seen at the Jersey City Medical Center Gastrointestinal Clinic or in private practice. Their symptoms were referable to functional or organic disorders of the colon. In 44 patients the diarrhea, pain and distention were of a functional nature and a diagnosis of spastic and irritable colon or mucous colitis was made. Thirty-four individuals had organic colon disorders: ulcerative colitis in 16, ileitis in 3, and infectious gastroenteritis in 15. There was one case of gastrogenous diarrhea.

Cantil was given alone, or in combination with phenobarbital when patients appeared tense and anxious. Doses were primarily of the order of 25 to 50 mg. four times daily with 12.5 mg. three or four times daily serving as the usual maintenance dose. When phenobarbital was given with Cantil, a single tablet was administered in which 25 mg. of Cantil was combined with 16 mg. of phenobarbital. Adjunctive medication with ACTH or prednisone was employed principally in cases of ulcerative colitis and with antibiotics and opiates in cases of infectious gastroenteritis.

Results of therapy are summarized in Table I.

Results in Functional Colon Disorders

In this group of 44 patients, Cantil successfully controlled diarrhea, distention and pain in most instances. In 26 of these patients with functional disorders, diarrhea was the principal complaint. The great majority were maintained symptom-free for from three months to a year with Cantil with phenobarbital three times daily. Only rarely did an acute exacerbation of severe diarrhea occur. Two cases of diarrhea with rectal bleeding were managed with ACTH or prednisone or both. When the acute attack subsided, these two patients were again maintained satisfactorily on Cantil with phenobarbital.

There were 18 patients with pain and distention as their chief complaints. In 6 the symptoms were completely controlled by Cantil. In 8 the symptoms were partially controlled so that they felt well most of the time, particularly when Cantil with phenobarbital was given. Four patients did not respond to therapy.

One patient with gastrogenous diarrhea due to achlorhydria was treated initially with ACTH and Cantil. Following this, longterm therapy with Cantil, 25 mg. four times daily, kept the diarrhea completely under control. Diarrhea recurred when Cantil was discontinued.

Results in Organic Colon Disorders

Cantil was found very helpful in management of ulcerative colitis, reducing the frequency of bowel movements, enabling solidification of intestinal contents into formed stools, and checking hemorrhage. Its usefulness, like that of other anticholinergic agents, is adjunctive to such classic measures as rest, diet, antibiotics, chemotherapeutic agents, corticosteroids, and psychotherapy. Frequently, therapy with Cantil in conjunction with ACTH or prednisone resulted in complete restoration of normal bowel function. Abdominal cramps disappeared, signs of rectal pathology cleared, and the patients responded with an increase in weight and an improved sense of well being. Despite these favorable clinical results, however, roentgenographic studies of the colon following oral barium or barium enema failed to disclose any definite changes.

Of 16 patients with ulcerative colitis, 14 were managed medically while 2 required surgical intervention because of hemorrhage in one instance and obstruction in the other. Drug therapy consisted of Cantil or Cantil with phenobarbital in 6 cases and either preparation in combination with ACTH or prednisone in 8 cases. All of the 14 cases are now on long term follow-up involving periods of 6 to 18 months and have remained in good condition on maintenance doses of 12.5 mg. of Cantil with or without phenobarbital, three times daily. Bowel movements are normal. Proctoscopic findings are normal or improved.

Most of these 14 patients with ulcerative colitis experienced mild to moderate recurrent episodes of diarrhea at varied intervals, in some instances accompanied by rectal bleeding. In 3 cases, these recurrences were severe. All acute episodes were immediately treated with ACTH or prednisone until brought under control. Once remission was apparent, the patients were placed on a Cantil regimen.

In 3 cases of ileitis treated with Cantil no appreciable control of diarrhea was achieved.

In the 15 cases of viral or bacterial gastroenteritis treated with Cantil with phenobarbital an attempt was made to identify invading organisms. Proper antibiotics were given where invading bacteria were found. Symptomatology common to the group included abdominal pain and cramps, distention, flatulence, and marked generalized malaise. Watery stools were passed 6 to 20 times daily. Most cases were treated with an intestinal antibiotic for 5 to 7 days although one patient required such medication for a period of 3 weeks. Ten patients required varied amounts of opiates to help control the severe diarrhea. All cases of long duration were controlled partially or completely by Cantil, 25 to 50 mg. four times daily, after the acute stage had subsided. Patients were kept on Cantil as long as required, up to 3 months in several instances.

Side-Effects

While Cantil was studied with reference to its efficacy in relieving the symptoms of colon disorders, particular attention was given to its apparent selectivity for the colon as indicated by pharmacologic studies. This latter attribute promised beneficial effect on the colon with little or no clinically significant action elsewhere, so that such typical anticholinergic side-effects as urinary retention, blurring of the vision and dryness of the mouth would not interfere with therapy. With Cantil, these side-effects were no problem. It was interesting to note that patients with ulcerative colitis are more likely than others to experience side-effects. While blurred vision and dryness of the mouth occurred in a few cases, reduction of dosage to half of a tablet (12.5 mg.) three to four times daily eliminated the side-effects. One case of ulcerative colitis was definitely benefited by Cantil, 75 mg. four times daily, and had no side-effects. In functional diarrhea as much as 50 mg. four times a day could be given without side-effects. No clinically significant side-effects were encountered in patients with functional diarrhea, irritable or spastic colon, infectious gastroenteritis, ileitis and gastrogenous diarrhea. In two instances there was urinary retention. On smaller dosage one case was able to continue with Cantil; the other, a known prostatic case, was unable to continue.

Case Reports

Case 1:—M. F., female, age 49 years, had been under treatment for a period of 8 years due to frequently recurring attacks of abdominal pain and diarrhea referable to an irritable or spastic colon. During this period of time she had been treated with a variety of drugs. She was placed on a regimen of Cantil, 25 mg. four times daily. Results of therapy were excellent. Complete relief of pain and diarrhea was achieved with no side-effects.

Case 2:—G. E., male, age 38 years, with symptoms of irritable or spastic colon: alternating bouts of diarrhea and constipation associated with lower abdominal and back pain and with cramps. Rectal bleeding occurred because of hemorrhoids. Treatment with 25 mg. doses of Cantil three times daily gave excellent relief of symptoms. No side-effects were observed.

Case 3:—M. G., male, age 52 years, suffered from abdominal pain associated with symptoms of "indigestion", constipation and distention. A diagnosis of irritable or spastic colon was made and treatment with 25 mg. of Cantil four times daily initiated. Excellent control of symptoms is now maintained with Cantil with phenobarbital three times daily. This patient experienced no side-effects.

Case 4:—D. C., female, age 28 years, is a case of ulcerative colitis with symptoms of abdominal cramps, diarrhea with passage of watery stools, mucus, and blood. She was treated with ACTH during the acute phase of the disorder

and subsequently placed on Cantil, 10 mg. three times daily. On this dosage, bowel function was returned to normal so that one full bowel movement of normal consistency occurs daily. At this time, the patient has been maintained

TABLE I

RESULTS OF TREATMENT WITH CANTIL IN FUNCTIONAL AND ORGANIC COLON DISORDERS

Diagnosis	Prominent Symptoms	No. of Patients	Response to Therapy		Remarks
			Control of Symptoms	No Relief	
Functional Diarrhea, Irritable or Spastic Colon	Abdominal pain, diarrhea, constipation, distention	44	40	4	Adjunctive ACTH or prednisone therapy in 2 cases. No side-effects
Ulcerative Colitis	Abdominal cramps, diarrhea, mucus and blood in stools	16	14	2	Adjunctive ACTH or prednisone therapy in most cases. Blurring of vision, dryness of mouth in a few cases: treatment discontinued in 1 patient because of nausea.
Ileitis	Diarrhea	3	0	3	No side-effects.
Infectious Gastro-enteritis	Abdominal pain and cramps, diarrhea, flatulence, generalized malaise	15	15	0	Antibiotic given initially; in 10 cases, opiates given adjunctively to control diarrhea. Minimal blurring of vision, dryness of mouth: controlled by reducing dosage.
Gastrogenous Diarrhea	Diarrhea	1	1	0	No side-effects.

for a period of one month on 12.5 mg. of Cantil three times daily without side-effects.

Case 5:—A. H., female, age 41 years, has a 20-year history of ulcerative colitis manifested as diarrhea with passage of watery stools, mucus and blood

alternating with occasional constipation. This patient also has bleeding hemorrhoids. She has been seen for several months during which she has been given Cantil in varied doses, ranging from 10 mg. every four hours to 25 mg. four times daily. The patient complained of blurring of vision with doses of 25 mg. four times daily. When she was given Cantil with phenobarbital, three times daily there were no side-effects. On this regimen, diarrhea and bleeding have been checked and the patient no longer has a sensation of gas in the rectum.

Summary

N-methyl-3-piperidyl-diphenylglycolate methobromide (Cantil), a new piperidol anticholinergic, was appraised for its ability to control or eliminate symptoms and for its freedom from side-effects in 79 patients with functional and organic colon disorders.

In 40 of 44 cases of irritable or spastic colon, Cantil or Cantil with phenobarbital reduced or abolished abdominal pain, diarrhea and distention and promoted restoration of normal bowel function.

Given in conjunction with ACTH or prednisone in ulcerative colitis, Cantil alone or with phenobarbital helped effect remissions of diarrhea and cramps in 14 of 16 patients, followed by an increase in weight and an improved sense of well being.

Cantil with and without phenobarbital proved a valuable adjunct in treatment of 15 cases of infectious gastroenteritis.

No appreciable benefits were apparent when Cantil was given to 3 patients with ileitis.

Usual therapeutic doses were 25 to 50 mg. and maintenance doses were 12.5 mg. of Cantil, given three to four times daily. Tablets of Cantil with phenobarbital, each containing 16 mg. of phenobarbital in addition to Cantil, were used where there was obvious tension and anxiety.

Cantil proved to be singularly free of anticholinergic side-effects. Blurring of vision or dryness of the mouth were occasionally seen and were usually managed with a reduction in dosage. Urinary retention, noted in two cases was eliminated in one by reducing dosage.

Conclusions

Cantil relieves or reduces diarrhea, distention and pain in many patients with functional and organic colon disorders. It is singularly free of the side-effects commonly encountered with anticholinergics. Blurring of vision and dryness of the mouth occur rarely, and may usually be eliminated by reduction in dosage. Urinary retention was encountered in two cases.

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THE DUMPING SYNDROME: A REVIEW

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Gastric surgery is followed occasionally by unforeseen complications that sometimes prove more troublesome than the original condition for which the operation was recommended. These postgastrectomy complications may include: failure of the gastroenterostomy stoma to function, difficulties of the afferent loop, postgastrectomy loss of weight, marginal ulcer, macrocytic anemia and a group of postcibal symptoms referred to as the "dumping syndrome". The dumping syndrome is a symptom-complex that may be very important in the postoperative management of postgastrectomized patients and usually becomes the problem of the gastroenterologist or the internist. There is a great deal of confusion in the literature concerning the dumping syndrome and we would like to present our concept of this problem and review the pertinent literature in an attempt to dispel the confusion and contradictions.

First of all, it is very important to clarify what is meant by the dumping syndrome. In many patients, soon after gastric resection, digestive symptoms appear during or immediately after eating. Epigastric pain or a feeling of lower substernal distention is due to over-filling of the gastric remnant, usually disappears in several weeks or months, and can be prevented by eating small meals. This is not the dumping syndrome nor is another group of symptoms which is referred to as the afferent-loop syndrome[1,2], and consists of the vomiting of bile, sometimes without food, but usually occurring 10 to 45 minutes after meals. The vomitus is bitter-tasting, bile-stained or colorless and represents regurgitated bile and pancreatic juices accumulated in the duodenum and afferent jejunal loop because of a mechanical difficulty in the anastomosis. In some cases the afferent loop fills with food from the gastric stump and there is vomiting of the secretions and food[1]. These symptoms of afferent loop stasis and bilious regurgitation usually do not persist after the first few postoperative months, when the edema at the anastomosis site subsides. It must be recognized that the above two conditions are not the "true" dumping syndrome although some of their symptoms may be part of the symptomatology of the dumping syndrome which must always include a group of vasomotor symptoms to be discussed later.

The dumping syndrome has been classified into two types, the early postprandial and the late postprandial. In the light of present knowledge the "late

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dumping syndrome" has been termed postgastrectomy hypoglycemia[1]. Postgastrectomy hypoglycemia ("the late dumping syndrome") will be discussed briefly and the remainder of our discussion will be limited to the early postprandial dumping syndrome, the more frequent of the two and the more controversial of the two. It is well to remember that both may occur in the same patient[3].

The "late dumping syndrome" (postgastrectomy hypoglycemia) is less frequent than the early type[4], occurs two to three hours after a meal and consists of weakness, sleepiness, sweating and nervousness. It is generally agreed that these symptoms are associated with hypoglycemia blood levels. In one study[5] one-third of postoperative ulcer patients had blood sugar levels below 40 mg. per cent during a five-hour glucose tolerance test although not all had symptoms. These symptoms can be relieved by the ingestion of sugar or sweetened food, but a patient with the late dumping syndrome should be maintained on a diet high in protein and fat and low in carbohydrate.

At the present time the early dumping syndrome is considered to be "a group of postcibal symptoms appearing after operation upon the stomach in which the pyloric sphincter is either removed (gastrectomy) or by-passed (gastroenterostomy)"[1] resulting in an altered passage of food from the stomach into the small intestine. These symptoms appear several days to several weeks after total gastrectomy, partial gastrectomy or gastroenterostomy. The symptoms in order of frequency are: weakness, nausea, epigastric distress, eructations, perspiration, sense of warmth, desire for bowel movement, sighing, vomiting, dizziness, diarrhea, drowsiness, desire to lie down and relief after lying down. The objective signs are: flushing (occasionally pallor), dilated pupils, tachycardia, sweating, and fluctuations in blood pressure (usually elevated but sometimes lowered). It is evident that[4] many of these symptoms and all of the signs are characteristic of vasomotor involvement. They appear after all meals in some individuals and only after certain meals in others. Most patients complain of the symptoms after the heaviest meal of the day, particularly dinner; others after meals containing sweets, milk or fluids. The symptoms start during the meal or shortly after, usually within 10 to 30 minutes, last 30 to 45 minutes and gradually subside. Many patients curtail their caloric intake because the ingestion of food causes discomfort. They gradually lose weight and may develop evidences of malnutrition such as hypoproteinemia, edema and vitamin deficiency. The symptoms of the dumping syndrome are worse during periods of emotional stress and strain and improve during periods of calm[4].

Incidence

The exact incidence of the early dumping syndrome is difficult to ascertain from the literature because of the confusion in terminology and classification and because most cases are mild and transient occurring when the patient

resumes taking food by mouth postoperatively. Many of these disappear within a few days, especially if fluids are eliminated at mealtimes. Many clear up in about six to nine months. Goligher and Riley[6] studied 224 patients after total and subtotal gastrectomy, noting that six months postoperatively 12.5 per cent had a severe dumping syndrome but 18 months postoperatively this was reduced to 7.1 per cent. Mills[7] in a postoperative study of 364 gastrectomies found that 22.8 per cent suffered from some degree of the dumping syndrome; 4.4 per cent had the more severe form and 18.4 per cent a milder form. Other observers[1,8] report that from 5 to 15 per cent of patients after gastric surgery have a severe and fairly persistent form, but it is generally agreed that about 2 per cent[9] of

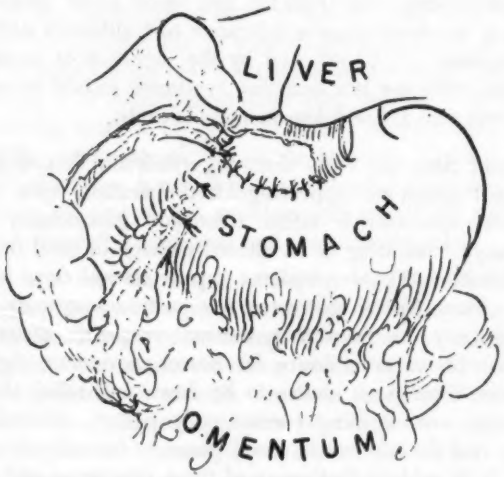

Fig. 1—Diagrammatic sketch of Billroth I operation. From: Welch, Claude E., *Surgery of the Stomach and Duodenum*, Second Edition, 1955, The Year Book Publishers, Inc., Chicago, Ill.

postoperative patients get it in a form that is so severe and persistent that it becomes disabling.

Etiology

There have been a multitude of theories offered for the pathogenesis of the early dumping syndrome and there is no generally accepted explanation for the mechanism of its production. The term "dumping" was given to this condition because it was considered due to the rapid dumping of food from the stomach into the unprepared jejunum. Some of the early theories offered were: 1. increased gastric motility with rapid emptying of a small gastric remnant and with rapid jejunal filling and distention, due to the absence of a sphincteric mechanism between the stomach and small bowel[10,11]; 2. delayed

emptying of the stomach remnant[12]; 3. reflux of food into the afferent loop of the anastomosis and into the duodenum[13]; 4. hyperglycemia due to rapid absorption of carbohydrate[14]; 5. reactive hypoglycemia subsequent to the initial hyperglycemia due to the similarity of the symptoms of the dumping syndrome with those of hyperinsulinism[15,16] and 6. jejunitis[17].

"A review of the literature on the dumping syndrome shows the confusion that comes from many conflicting reports"[1]. Many theories have been offered as to the causation of these symptoms by competent observers who report their

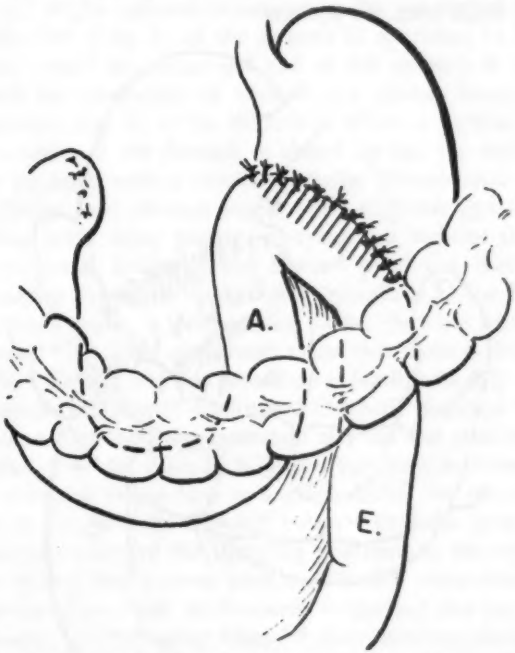

Fig. 2—Diagrammatic sketch of Polya modification of the Billroth II operation. From: Welch, Claude E., *Surgery of the Stomach and Duodenum*, Second Edition, 1955, The Year Book Publishers, Inc., Chicago, Ill.

experiments to support these theories, most of which can be grouped into four categories: mechanical, osmotic, electrolytic and psychosomatic. It is probable that in an individual case any one or all of these mechanisms may be involved.

Mechanical Theory

The British workers have been the main proponents of the mechanical theory. Wells and Welbourn[2] believe that after partial or complete removal of the stomach, food passes readily into the small intestine without having been

diluted, mixed with gastric juice or acidified. The jejunum receives the bolus precipitously, rather than in continuous small amounts. A large bulk of the food entering the jejunum hurriedly results in increased bowel activity. Increased intestinal tension results, which, in turn, stimulates efferent splanchnic nerve endings in the intestinal wall and causes the symptoms of dumping. Wells and Welbourn[2] term this the efferent-loop syndrome (the same as the early dumping syndrome), "the commonest of postgastrectomy syndromes"[2], as distinct from the afferent-loop syndrome. They point out that hypertonic solutions are particularly troublesome because the bulk of the intestinal contents is increased by the diluting fluids from the jejunum.

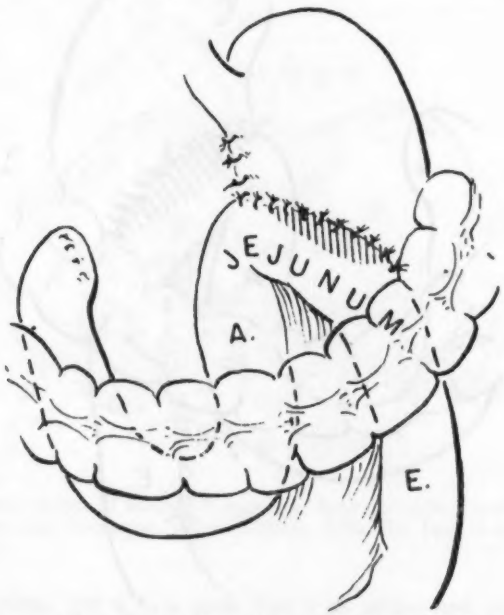

Fig. 3—Diagrammatic sketch of Hofmeister modification of the Billroth II operation. From: Welch, Claude E., *Surgery of the Stomach and Duodenum*, Second Edition, 1955, The Year Book Publishers, Inc., Chicago, Ill.

Butler and Capper[18] maintain that the early dumping syndrome is caused by the weight of the gastric contents plus the weight of the afferent loop which results in a drag on the gastric remnant, in turn causing excessive sympathetic stimulation and vasomotor changes. Lying down causes the vasomotor symptoms to disappear within about five minutes. They produced these symptoms in 79 patients by placing a mercury-filled bag in the gastric stump. These symptoms could be checked by a splanchnic block and this was considered indicative of the symptomatology being due to impulses released through the sympathetic

nervous system. Goligher and Riley[6] disagree with this theory on the basis of their observation that the dumping syndrome becomes more frequent when increasingly larger portions of the stomach are removed and is thus more frequent after total gastrectomies, but they were able to produce symptoms of dumping by inflating a balloon placed in the jejunum under x-ray control.

There have been many investigators who have studied the effect of various gastric operative procedures in the production of the early dumping syndrome. The basic gastric resections for peptic ulcer are the Billroth I operation (Fig. 1) where the cut end of the stomach is sutured to the cut end of the duodenum, the Polya modification (Fig. 2) of the Billroth II operation (a more extensive gastric resection) where the entire cut end of the stomach is anastomosed to the jejunum with the production of afferent and efferent loops, and the Hofmeister modification (Fig. 3) of the Billroth II where a portion of the cut end of the lesser curvature of the stomach is closed up and the remainder is anastomosed to the jejunum, with a resultant smaller gastrojejunal stoma but still retaining the afferent and efferent loops. Most surgeons agree that the Hofmeister procedure helps delay gastric emptying and reduces the incidence of the dumping syndrome. Zollinger and Hoerr[16] point out that a majority of cases of the dumping syndrome appear after operations of the Polya type with a large gastrojejunal stoma, a predisposing factor that has also been stressed by other observers[18,19,20]. Some observers[21] claim that there is little or no dumping following the Billroth I but this procedure is feasible in only a small number of cases that require resection[20]. Butler and Capper[18] observed 79 cases of the dumping syndrome after the Polya operation and not one case after the Billroth I. In a recent study[22] of 291 cases of Billroth I resection, however, symptoms of dumping were observed at one time or another during the postoperative period in 34 per cent of the patients. O'Neill[20] believes that the greatest factor contributing to the production of the dumping syndrome is the type of operation with the Polya giving the greatest number. Strode[21] recommends making the gastrojejunal stoma 3 to 4 cm. in diameter to prevent the rapid emptying of the gastric remnant. At the Lahey Clinic[9,23] they attribute their low incidence of the dumping syndrome to the practice of doing the antecolic Hofmeister type of anastomosis with a small stoma and producing an angulation of the efferent loop, thus effecting a trapping device and preventing rapid gastric emptying and hyperdistention of the jejunal loops. O'Neill[20] has proposed a modified Billroth I with a valvular anastomosis between the jejunum and gastric stump, and claims a reduction in the incidence of the dumping syndrome following this procedure. Fisher[19] points out that dumping is directly related to the degree of disruption to which gastrointestinal continuity is subjected, being least with vagotomy and pyloroplasty, intermediate with Billroth I and greatest with Billroth II (Polya). Other observers[1,6] believe that the incidence of dumping is not related to the type of gastrectomy but is more pronounced the more extensive the resection, with a greater frequency after total gastrec-

tomy. Moloney[24] reviewed the results of a series of 154 cases operated on for peptic ulcer and compared the Billroth I and Polya technics. It was found that after Billroth I the patients showed fewer and less persistent dumping symptoms.

Osmotic Theory

The observations and experiments of Machella[4,25,26,27], indicate that the symptoms of the early syndrome are due to the distention of the jejunum by fluid which enters the lumen of the gut from the blood stream in response to the presence of a hypertonic solution formed by the ingredients of a meal possessing osmotic properties and are not due to distention by the original bulk of the ingested food. These symptoms are not caused by hyperglycemia, although a hyperglycemia may be present during the period of symptoms. He studied 16 patients with the dumping syndrome following subtotal gastrectomy and found that the symptoms occurred toward the end of a mixed meal or shortly thereafter, during which time the blood sugar concentration was always elevated. These symptoms were accompanied by a rise in blood pressure and an increase in pulse rate. Hypoglycemia was not found in any of the patients during the period of symptoms. The typical symptoms of the dumping syndrome were reproduced by the administration of glucose and sucrose orally but not when glucose was given intravenously. He produced the symptoms of the dumping syndrome in individuals with intact stomachs, as well as in patients with subtotal gastrectomies, by the intrajejunal installation of hypertonic solutions of glucose, protein hydrolysate and sodium sulfate and by distention of the jejunum with an air-inflated balloon. These symptoms have also been observed by him when he introduced concentrated solution of magnesium sulfate into the duodenum for the purpose of evacuating the gallbladder. Included among the above are substances that obviously do not cause a hyperglycemia. To cause symptoms of the dumping syndrome the ingested food must be capable of exerting osmotic pressure, such as sugar, electrolytes or protein products. Enough fluid must be ingested during the meal to dissolve the ingredients possessing osmotic properties and yet form a hypertonic solution of sufficient strength to draw additional fluid from the blood stream into the gastrointestinal tract. Machella also points out that the dumping syndrome is sometimes encountered in individuals receiving intrajejunal feedings if the material enters too rapidly, and occasionally after a heavy meal in individuals with a very rapid gastric emptying time. He mentions that it is well to keep in mind the possibility of postprandial hyperglycemia and glycosuria in postgastrectomized nondiabetic individuals.

Zollinger and Hoerr[16] were unable to evoke the symptoms of the dumping syndrome by means of a balloon in the jejunum but they agree, however, that abnormal sugar absorption takes place in patients with dumping symptoms and that these symptoms occur during the hyperglycemic phase. Fisher[19] has confirmed the main points of Machella's experiments and observations but Glaze-

brook and Welbourn[28] failed to find any dilatation of the jejunum when symptoms of dumping were present. Roberts and his co-workers[29] also have cast doubt on Machella's theory of jejunal distention but found a fall in blood volume, accompanied by electrocardiographic changes, after the administration of hypertonic solutions to gastrectomized patients who had dumping symptoms. They believe that the dilution of hypertonic solutions in the jejunum results in a shift of extracellular water and probably electrolytes as well, causing an acute drop in blood volume, which they feel is the main etiological factor in the dumping syndrome. Their experiments revealed that the fall in blood volume did not occur when the jejunum was distended by a balloon or by the rapid administration of isotonic fluids without osmotic effect. Hayes[3,30] compares the dumping syndrome to a vasomotor shock-like complex (tachycardia, palpitations, perspiration, dizziness and nausea) and believes it is due to rapid introduction into the jejunum of a hyperosmolar mixture which is rendered isotonic by the withdrawal of water from the circulating blood producing an acute reduction in effective circulating blood volume. It is perhaps significant that patients with the dumping syndrome get relief after lying down, a situation not unlike that seen during the early stages of shock. Munck[31] of Copenhagen points out that there is a great resemblance between the early stages of shock, when the sympathetic tonus is increased and the symptoms in a pronounced attack of dumping (rise in blood pressure, tachycardia, vasomotor symptoms, sleepiness and fatigue) which has all the appearance of a hyperactivity of the sympathetic nervous system.

Electrolyte Theory

More recently the role of the potassium ion in the dumping syndrome has been investigated. Smith[32] in England confirmed Machella's observation of the over-rapid entry into the jejunum of hypertonic food but states that this causes a fall in the serum potassium. He ascribes this to the rapid emptying of the stomach which causes an abnormal rise in blood sugar. He further suggests that two mechanisms contribute to this potassium ion lack—the release of some adrenalin-like substance into the blood and rapid absorption of ingested carbohydrate leading to rapid deposition of glycogen with the binding of K^+ inside the glycogen storing cells. Kleinman and Grant[8] in this country have carried Smith's work further and believe it is of utmost importance. They agree with Smith[32] that blood sugar curves in "dumpers" climb sharply and fall rapidly after a meal, especially one rich in carbohydrates. The attack occurs during the hyperglycemic phase and the serum potassium falls significantly during the attack and returns to its fasting level by the end of the episode. Some electrocardiographic changes occur: shortening of the QT interval and depression of T-waves, which they interpret as consistent with hypopotassemia. They suggest that the dumping syndrome is caused by the sudden shift of K^+ from the extracellular fluid into storage in the liver with glucose. The sudden shift

causes a transient hypokalemia and the clinical symptoms are presumably the result of this hypokalemia. The symptoms recede when sufficient K^+ is released from cellular storage to correct the extracellular deficiency. They agree with Smith[32] that an adrenergic imbalance is the probable cause for the abnormally rapid deposition of glucose in patients subject to the dumping syndrome. In view of this they treated ten patients with ten grains of enteric coated potassium chloride 20 minutes before meals and they become symptom-free. A criticism of their work is the short follow-up the authors report on these patients, and they themselves admit that their laboratory data did not agree with the above idea. The blood surgar curves were lower than expected and usually reported in the literature in patients with dumping and the serum K^+ failed in all but two cases to follow the predicted pattern. They feel, however, that the clinical evidence completely supports this theory. Munck[31], on the basis of his experiments, excluded hypopotassemia as a factor and was of the opinion that the electrocardiographic changes were due to increased sympathetic tonus.

Psychosomatic Theory

At this point it is timely to review Alvarez'[33] ideas on the dumping syndrome. Back in 1949, before most of the above work was done, he wrote that the dumping syndrome is not dependent on the presence of a gastroenteric anastomosis or a gastric resection. He felt that the symptoms were reflex and due to mechanical, physical and chemical stimulation of the jejunal mucosa and that he could produce it by running food into a jejunal fistula—too rapid, too cold, or too concentrated in sugar. He suggested that an especially unstable nervous system might be an essential etiological factor. He reported that the dumping syndrome could be seen in hypersensitive, overly-reactive or psychoneurotic persons who had not had any operation on the stomach and in these persons he attributed the symptoms to a rapid outpouring of food through a patulous pylorus. He reported two such cases in highly neurotic individuals who had never had any gastric surgery. The factor of emotional tension and psychiatric stigmata as predisposing agents has been agreed upon by many observers[11,34,35] and this may be in line with the theory of the unstable vasomotor system and increased sympathetic tonus as factors in the production of the dumping syndrome. It is interesting to recall that Butler and Capper[18] caused the temporary disappearance of the dumping syndrome by infiltrating the lumbar sympathetics with 1 per cent procaine and Machella[25] reported that intravenous etamon has been able, in some instances, to prevent the usual reactions to hypertonic solutions in his patient with dumping syndrome.

Prevention

The question of prevention has been discussed in the section on surgical procedures. Although "there is little agreement on the operative procedures to be used"[2] it is generally agreed that the more extensive the gastric resection,

the greater are the chances of developing the dumping syndrome. "A lesser resection, however, may be inadequate and may predispose to marginal or jejunal ulcers. Perhaps a lesser resection (50 per cent) and vagotomy may meet the requirements of acid reduction and large enough gastric remnant"[1]. It is also agreed that a smaller gastrojejunal stoma[13] will help reduce the incidence of this complication, if a more extensive gastric resection is indicated. Machella[4] in his most recent paper reverses his previous ideas[25] and states that the surgery of gastric resection should be performed in such a manner as to preserve sufficient reservoir function of the gastric remnant in order to allow ingested food to leave the gastric stump slowly. Various modifications of standard surgical procedures have been suggested to decrease the flow of gastric contents to the jejunum and the more important have been mentioned above.

Treatment

Ross[23] points out that it is probably an excellent idea to anticipate the possibility of this syndrome early postoperatively in tense, anxious individuals and start them immediately, but gradually, on the program outlined below. All patients when they leave the hospital after a gastrectomy should be told that at first they must take small solid meals at frequent intervals and chew their food well. They must be assured that during the next few months they will be able to eat more and more until they are taking normal meals.

The treatment of this syndrome consists of meals of low residue, given initially in small feedings at intervals of two hours with reduction of fluids by mouth at mealtime. Fluids are given between meals. The feedings are kept as dry as possible to delay gastric emptying. A piece of dry toast may initiate the meal. Sugars should be limited. Milk is frequently not tolerated. The patient should be advised to eat slowly and take his food at body temperature. It has been suggested[33] that meals should be taken while the patient is reclining quietly. The patient should certainly lie down for a short while after meals if this is at all possible. Machella gives 1/50 or 1/100 grain atropine sulfate one-half hour before meals and claims good results with this, although others[3,10] disagree. The new blocking agents, like banthine, may be tried. Sedation of course is important when indicated. Reassurance and explanation are important adjuncts in management and often help relieve symptoms. Kleinman and Grant[8] treat their patients with 10 grains enteric coated potassium chloride 20 minutes before meals in line with their theory of hypokalemia.

A high fat, moderately high protein and low carbohydrate diet in a ratio of 5:1.5:1 has been suggested recently by Hayes[3,30] and this principle has been agreed upon before[16,21]. The high fat diet is proposed to inhibit gastric evacuation and together with a high content of protein, which is slowly hydrolyzed, should be fed to the maximum exclusion of carbohydrate, which is easily hydrolyzed. Hayes feels that this will help control the diarrhea, which is a

serious complaint in some patients, and is mediated through vagi by the sudden distention of the small bowel which stimulates a peristaltic rush.

As far as surgical correction is concerned, little can be said in favor of this form of treatment. It should not be considered unless the symptoms are severe, have persisted for at least 12 to 18 months and the patient has become a psychiatric and nutritional problem. It has been stated that a Polya can be converted to a Billroth I type of anastomosis "but technically this may be difficult"[2]. Attempts have been made to secondarily decrease the size of the gastrojejunal stoma but the results have not been encouraging. Interposition of the jejunal loop as proposed by Henley[36] seems to hold some promise as a corrective measure.

Conclusions

1. Although the dumping syndrome is common in the immediate postgastrectomy period, the severe, persistent and disabling form has a low incidence.

2. The true early dumping syndrome is characterized by a vasomotor complex which may be related to a mild, early shock-like state, secondary to temporary reduction of the circulating blood volume.

3. Mechanical, osmotic, electrolyte and psychosomatic theories have been postulated as the basic etiological factor in the dumping syndrome.

4. Dietary and medical management, explanation and reassurance give relief in most cases of the dumping syndrome.

5. Surgical therapy is only considered in refractory cases and up to the present is unsatisfactory.

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SOME NEWER OBSERVATIONS IN SMALL BOWEL OBSTRUCTION*

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The remarkable progress in surgery during the past half century has passed successively through three basic phases. A master surgeon of the past generation founded his surgical excellence upon a knowledge of anatomy. His surgical counterpart of yesteryear based his surgical mastery on pathological disturbances as revealed in clinical symptomatology. The modern surgeon has travelled the roads of anatomy and pathology as necessary corollaries to the completion of surgical basic training. A present day surgeon, attuned to the progressive tempo of the day, builds his superiority upon an interpretation of normal and abnormal physiology. Surgeons now speak and write in terms of physiology, biology, physiological and biological chemistry.

Application of this newer surgical concept to small bowel obstruction brings to our attention some newer observations on this subject. These experimental and clinical notations fall into the following major categories:

1. The pathways taken by an obstructed intestinal loop.

2. The lethal nature of obstructed bowel contents.

3. The axiom of distention and deflation ratio.

4. Physiological recovery as evidenced by x-ray.

5. Roentgenological criteria for intubation.

6. The significance of the serosal arterioles in the resuscitation of the small bowel.

7. Oxygen stimulation to intestinal peristalsis.

1. Obstructed pathways:—Small bowel obstruction finds its source of origin in one of three sites or a combination thereof. These obstruction points originate either within the bowel wall (e.g. tumors), inside the bowel lumen (e.g. intraluminal calculus) or outside the bowel itself (e.g. extraluminal postoperative adhesions). When in the course of normal small bowel physiology, this situation exists, the peristaltic activity of the intestine by an inherent phenomenon results in the pursuit of one of two pathways by the proximal unobstructed bowel loop. This segment of bowel may attempt to pass the obstruction by a transient increased peristaltic hyperactivity which produces a symmetrical distention and hypertrophy of the loop simulating a balloon. This process con-

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tinues proximally as long as the obstruction persists or until a complication such as a perforation results.

The other pathway pursued by the small bowel is to try to bypass the obstruction. This occurs when peristaltic activity propels the proximal intestinal loop to move to the right or left of the obstructing site or the loop attempts to go above or below it. This type of activity produces a volvulus or multiple twists in the small bowel segment or segments involved. This is the type of obstruction which usually results in embarrassment to the mesenteric vessels with gangrenous bowel as the inevitable termination.

2. *Lethal bowel contents:*—When one or more loops of small intestine become markedly distended a point is reached wherein the bowel wall no longer remains impervious to the intraluminal contents. The intestinal contents then commence to seep through the intestinal wall and enter the peritoneal cavity. A "shock-like" picture simulating incipient peritonitis results and as the process continues the inevitable symptom-complex of diffuse peritonitis supervenes.

Qualitative analytical studies on the intestinal contents taken from obstructed loops of small bowel have indicated that the predominating material therein are products of protein hydrolysis. More specifically these protein derivatives are:

a. Proteoses (probably heteroproteose).

b. Peptones (probably amphopeptone).

c. Polypeptides (probably a dipeptide).

These protein derivatives are the lethal constituents of the small bowel which, when injected into experimental animals, can produce shock and death[1]. Hence the old terminology of "toxins" resulting from intestinal obstruction can be explained on the basis of protein catabolism and the transposition of its products from an intraluminal to an extraluminal location.

3. *Axiom of distention and deflation:*—An observation of unprecedented interest has been made by serial scout films of the abdomen taken at 24-hour intervals. This phenomenon has been so consistent that I refer to it as an axiom. Stated in words this axiom is that *the distention rate in small bowel obstruction equals the deflation rate even as the duration of distention equals the duration of deflation.* To clarify this axiom hypothetical values are presented for exemplification. Thus, if it were to take an obstructed 12-inch loop of small bowel two weeks to become distended 4 inches (measured transversely); following the elimination of the obstruction, it will take that same loop of bowel approximately the same time (namely 2 weeks) to return to the diameter it had prior to the obstruction. Physiologically speaking, if two weeks have passed prior to the correction of an obstruction, it will

take two weeks following this correction for the intestinal segment to return to its former normal physiological activity. Following the elimination of the obstruction, diarrhea may develop in the patient several days later. This diarrhea becomes more intensified as the peristaltic activity returns to normalcy. The diarrheal fluid will be for the most part the material incarcerated within the obstructed loops of bowel. The odor of this liquid is foul smelling and typical of stagnant putrifying intestinal contents.

The axiom of distention and deflation is not applicable to the large bowel. On the contrary it has been noted in previous publications that in large bowel obstruction the cecum can become so distended that it can fill practically the entire abdominal cavity[2]. Cecostomy is mandatory under this circumstance. It has been observed, however, that the cecum will twist and form a volvulus in an attempt to bypass an obstruction similar to the small bowel as mentioned above[3].

4. Physiological recovery evidenced by x-ray:—The degree of return to physiological normalcy of obstructed small bowel can be ascertained by serial roentgenograms taken at 18 to 24-hour intervals. All that is necessary is a simple flat plate x-ray of the abdomen (scout film). A change in direction of the intestinal pattern on the x-ray film indicates an improvement in physiologic activity. The degree of improvement is directly proportional to the degree of change in position of the involved bowel segment. More specifically, the change is demonstrated when, for example, an initial x-ray film shows a classical step-ladder pattern which moves to a vertical position in one or several subsequent x-rays. If, following definitive treatment, an x-ray film shows distended loops of bowel to have altered position from a vertical distention to a horizontal one, then it can be assumed that the bowel is returning to its normal physiologic activity. This likewise is an indication of the process of anatomical restoration.

It must be emphasized that the change in bowel position via x-ray is a sign of improvement provided there is *not* an increase in the number of distended bowel loops. An increase in the number of bowel loops plus a change in position denotes a progression in the obstruction. Conversely a shift in position of obstructed loops with a diminution in the number of loops involved suggests an improvement in the bowel obstruction with a gradual return to function. As a theorem, it may be stated thus: A change in position of obstructed small bowel revealed by x-ray is a sign of physiologic improvement provided the number of loops involved remain the same or diminish in number. Contrariwise, a shift in position of obstructed small bowel loops plus an increase in the number of bowel segments indicates an intensification of the obstruction. The duration of the bowel distention will follow the pattern as discussed under the axiom of distention and deflation.

5. Roentgenological criteria for intubation:—An initial scout film will assist the operating surgeon in arriving at a decision to intubate or not to intubate the

patient with one of the longer type indwelling tubes (Miller-Abbot, Cantor, Grafton-Smith, etc.). If the x-ray shows that four or more distended prominent loops of small bowel are present, it is preferable to intubate because this is too much distended bowel to handle safely. Intubation decompresses the bowel and facilitates surgical manipulation. When not decompressed, distended bowel may perforate upon manual change of position and often can only be redeposited into the peritoneal cavity with much difficulty. At operation the surgeon can manage three or four distended loops; beyond that number he will have difficulty.

This same x-ray film which will assist in the decision of intubation may also be of value in another way. If the film shows a fan-like pattern (or a tendency to it) of the intestinal distention, then a hint is given as to where the obstruction originates. This site of origin will be opposite to the area showing the maximum distended bowel. Distending small bowel forms a pattern like a fan as the distention progresses away from the point of origin. Thus the incision for exploration would be made opposite to the fan-like pattern. Hence if the fan-like distention is in the right upper quadrant, the incision of choice would be in the left lower quadrant. Conversely, a pattern in the left upper quadrant would argue for an incision in the right lower quadrant, etc.

6. Significance of serosal arterioles:—On many occasions the surgeon is confronted with the problem of whether or not an intestinal segment is viable. At the operating table valuable time elapses as the surgeon waits patiently for an obstructed loop of bowel to return to normalcy. Since most patients with intestinal obstruction are not the best operative candidates, the additional period of anesthesia and exposure of the peritoneal cavity to the atmosphere increases the morbidity. Often this delay, lingering and waiting, may be a precipitating factor in the cause of death.

Thus a rapid diagnostic criterion of small bowel viability is of practical importance. A satisfactory criterion is available at the operating table by direct investigation of the vascular system of the obstructed loop. The point of observation is the distal circumference of the small intestine on the antemesenteric border. The serosal arterioles are examined for their red color and the presence or absence of pulsations. These vessels in normal intestine are not as prominent as they are in the obstructed loop with secondary venous congestion. The venous congestion increases the arteriolar pressure so that the vessels become extremely prominent. If pulsations are visible in the small arterioles on the antemesenteric border and if the red color of the circulatory blood can be seen, then the bowel is viable. This is true even if the intestinal wall is markedly darkened from edema and congestion and even if the blue-black color of the intestine is prominent[4].

The rationale of this observation resides in the fact that if there is adequate arterial circulation and venous return in the most distal area of the in-

testine the circulation must be satisfactory in the more proximal areas. Where there is adequate arterial circulation, there is adequate oxygenation with a satisfactory nutritional supply to the tissue under observation. Adequate oxygenation and nutrition of the segment are the basic necessities for intestinal viability. Both the physiologic functions depend upon a sufficient arterial circulation. Therefore, when an adequate circulation is present, the intestine must, of necessity, be viable. This criterion has been followed on many occasions at the operating table without any serious complications occurring which could be attributed to the intestinal segment under observation.

7. *Oxygen stimulation to peristalsis:*—One of the most effective methods of stimulating the small intestine to peristaltic activity is to administer oxygen via inhalation. For this reason oxygen should be given as a valuable adjunct in the therapy of adymamic ileus either as a primary pathological state or as a residuum to an obstruction. Conversely, the elimination of oxygen to the point of anoxia will result in an inhibition to small bowel peristalsis[6].

In any mention of the inhibition of peristalsis, secondary to oxygen insufficiency, it must be remembered that alterations in peristaltic activity do not depend on one factor alone. In the summation of those factors producing peristaltic inhibition secondary to oxygen depletion, however, the elimination of this oxygen depletion will accelerate bowel activity. Any inhibition of motor activity of the small bowel is not irreversible. Adequate oxygenation with eradication of the hypoxic state enables the intestine to return to normal physiologic activity. However, the persistence of anoxia to the point of tissue anoxia producing cell death results in a nonviable intestine which cannot be revived.

Summary

A resumé of the more current clinical and experimental observations on small bowel obstruction is presented and discussed. The major categories of the discussion concern the following:

1. The paths of least resistance taken by the small bowel when an obstruction is encountered.

2. The lethal nature of obstructed bowel contents.

3. The postulation of an axiom concerning the distention and deflation of obstructed intestinal loops.

4. The value of serial x-ray studies as an aid in the evaluation of physiological recovery of an obstructed bowel loop and as a criterion for intubation and as an aid in the choice of an operative incision.

5. The significance of the serosal arterioles as an indicator for small bowel viability.

6. Effects of oxygen on small bowel peristalsis.

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THE DIAGNOSIS AND TREATMENT OF CHRONIC REGIONAL ENTERITIS*

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Introduction

Twenty-five years ago Crohn and his associates[4] presented a discussion of their clinical and pathological studies of 14 patients with a disease of the small intestine which they called regional ileitis. At least a dozen descriptions of similar cases had been published before but their complete and careful studies established this disease as a clinical entity.

The world wide recognition of this disease, its surprising frequency and a tremendous interest among members of the profession has resulted in a voluminous literature. The original paper by Crohn and his associates[4], the concise and complete discussion by Boyce[2], the detailed and comprehensive study of Van Patter and his associates[6], the excellent chapter by Bockus[1] and Crohn's[5] brilliant monograph are source material and worthy of careful study.

Although this disease has extended beyond its original regional concept it is only fair to emphasize that little has been added to the symptoms, complications and course of the disease as described by Crohn and his associates[4].

Regional enteritis, a term more widely employed than regional ileitis, now includes acute regional enteritis, chronic regional enteritis, ileojejunitis, ileocolitis and rarely regional enteritis involving the duodenum and stomach.

In this discussion chronic regional enteritis is the main subject for consideration.

The etiology of regional enteritis remains obscure.

Diagnosis

The diagnosis of regional enteritis may be strongly suspected when there is an association of diarrhea, abdominal pain, fever and weight loss. If to these symptoms are added an abdominal mass in the lower abdomen and fistula formation—the diagnosis becomes more certain.

The diagnosis, however, is not a simple one. An important aid in the diagnosis of regional enteritis is to keep this disease in mind in any obscure abdominal disease characterized by crampy abdominal distress and diarrhea.

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In the physical findings the presence of an abdominal mass and fistula formation are significant findings. The abdominal mass consists usually of inflamed intestine, adherent loops of adjacent bowel and thickened mesentery. An abscess may be present within the mass.

A perirectal fistula may precede by months or even years the symptoms of regional enteritis. The significant history of crampy abdominal pain or slight diarrhea may come to light only after direct questioning and then studies of the colon and small intestine may reveal the presence of the underlying disease.

The most helpful and usually conclusive study is the roentgenographic examination. This should include both the barium meal study of the small intestine and the barium enema.

The most valuable finding is the string-sign, a term borrowed from a similar observation in the barim enema examination of the irritable colon.

While the string-sign is highly suggestive of regional enteritis it may also be found in ileocecal tuberculosis, carcinoid tumors of the small intestine, endometrial implants of the ileum, lymphosarcoma of the small intestine and malignant tumors of the cecum.

Other changes in the small intestine such as shortening and rigidity, distorted mucosal pattern, narrowing of one portion with dilatation of the proximal segment and ulceration, aid in establishing the diagnosis. The entire small intestine must be studied in order that skip areas should not be overlooked. All of these examinations must be done with a great deal of care and at times repeat studies are essential.

There is nothing conclusive in the blood picture or in the chemical analysis of the blood to aid in establishing a diagnosis.

Differential Diagnosis

The combination of diarrhea, abdominal pain, fever, anemia, weight loss, abdominal mass and fistula formation strongly suggest the diagnosis of regional enteritis, the absence of several or many of these significant clinical features and even the lack of roentgen findings in some cases should not definitely rule out the disease[2]. Regional enteritis should always be kept in mind in the differential diagnosis of any chronic undiagnosed diarrhea. Some patients with undiagnosed regional enteritis are treated for variable periods of time for functional diarrhea.

When fever is noted, and the diarrhea mild and abdominal pain minimal, the diagnosis of undulant fever or brucellosis has been made[2]. If joint pains are prominent and a murmur of the heart has been heard the disease has been confused with rheumatic fever and subacute bacterial endocarditis[2].

Other conditions that have to be ruled out in differential diagnosis include ulcerative colitis—particularly involving the right colon, tuberculosis, Hodgkin's disease, lymphosarcoma of the small intestine, sprue, and amebiasis.

Acute appendicitis often creates difficulty both in differential diagnosis and in treatment. The assumption that the presence of diarrhea in a patient with an acute abdomen automatically rules out an acute appendicitis is incorrect. In Boyce's[2] series of 7,613 patients with acute appendicitis 374 had diarrhea as a symptom and of these 18 died.

Fig. 1—Case 1.

Fig. 2—Case 2.

Treatment

In the therapy of chronic regional enteritis it is important to treat each patient as an individual problem. There is no rule of thumb and there is no therapy medical or surgical that is universally applicable.

The treatment starts with a very complete survey of the patient both clinically and with the aid of the laboratory to establish the general condition of the patient, the extent of the disease process and complications if present.

The decision then has to be made whether the immediate problem is medical or surgical recognizing the fact that such a decision may have to undergo revision depending on the patient's response to the recommended therapy.

Medical treatment consists of: 1. diet, 2. vitamins, 3. drugs, 4. blood transfusions, 5. roentgen therapy.

1. The diet should be high in protein, high in calories, low in fat and residue. Milk is usually not well tolerated. The patient must be encouraged to eat in order to maintain good nutrition.

2. The vitamins may be given orally or parenterally. These include Vitamin B-complex, crude liver extract and Vitamin K.

3. Among the drugs that are prescribed are the following:

Fig. 3—Case 3.

Fig. 4—Case 4.

a. The sulfonamides are used to eradicate secondary infection. Sulfasuxidine and sulfathalidine has been used in the past, azulfidine has been prescribed most recently with encouraging results.

b. Anticholinergic drugs are used to allay abdominal cramps and to reduce bowel activity. Pro-Banthine, Pathilon and others have been prescribed. Bentyl hydrochloride has been particularly useful.

c. Cortisone and ACTH have been disappointing and at present seldom used in the therapy of our patients with regional enteritis.

4. Blood transfusions have been employed in the anemic patient and preoperatively.

5. Roentgen therapy has been tried in several of our patients with disappointing results.

We have found as others have that in regional enteritis like in ulcerative colitis sympathetic care and understanding and support of emotional needs are an important part of general therapy[7].

Surgical treatment is indicated when conservative medical treatment has failed to maintain reasonable health for the patient with intestinal or rectal complications, strictures, fistulas, abscesses and perforations and for the patient with recurrent disease where medical treatment has failed to control symptoms.

Fig. 5—Case 5.

Fig. 6—Case 7.

There is a great deal of controversy as to what constitutes good surgical treatment for regional enteritis.

Some men prefer ileocolostomy after exclusion or side-tracking the proximal end of the involved intestine. This is claimed to have the advantage of a lower morbidity and mortality than any other procedure without a higher recurrence rate[7].

Others favor primary resection of the lesion with end-to-end anastomosis.

The attitude towards removal of the appendix is also of interest.

If at surgery the appendix is found to be normal and regional enteritis is present some favor the removal of the appendix to obviate confusion later, others fear that appendectomy favors fistula formation. If the appendix is obviously inflamed of necessity it must be removed.

One of the most discouraging aspects of the treatment of regional enteritis, whether medical or surgical, is the recurrence of the disease. The development of diarrhea, abdominal pain and fever is sufficient indication in a patient who has had weeks or months of fairly good health that the disease process has become reactivated or has developed a new site of activity. Usually the area of recurrence is proximal to the anastomosis in the surgically treated patient. Medical treatment is strongly advocated for the patient who has a recurrence but not infrequently surgery has to be done again and sometimes again.

The following records of personally observed patients are briefly reviewed.

Case 1:—D. C. A white male, age 14, had diarrhea with crampy distress. He had lost 60 pounds in weight in a few months. A rectal fistula had developed four months previously. Surgical treatment for the fistula proved of no benefit. Roentgen studies (Fig. 1) demonstrated the presence of the regional enteritis, suspected from the history and presence of the rectal fistula. A course of ACTH therapy did not improve the condition but actually seemed to cause a marked progression of the symptoms. An end-to-end eleosigmoidostomy was done. Pathologically active chronic ulcerative colitis and regional enteritis were found. The result of surgery to date has been very good.

Case 2:—M. Z. A white female, age 51, complained of diarrhea, weight loss, and weakness. Physical examination revealed a tender mass in the lower right quadrant. Roentgen studies (Fig. 2) disclosed regional enteritis involving the terminal ileum. An ileotransverse colostomy was done with resection of the terminal ileum, cecum and proximal transverse colon. A good clinical result was obtained.

Case 3:—J. S. A white male, age 40, developed abdominal pain, diarrhea and abdominal distention. In the history a rectal fistula had been found two years previously. Diarrhea was noted later. The diagnosis of regional enteritis was established on roentgen study (Fig. 3). A side-to-side ileotransverse colostomy with exclusion was done. The patient died four days postoperatively from a staphylococci septicemia.

Case 4:—F. P. A white male, age 28 was seen because of crampy pains, diarrhea and weight loss. The roentgen studies (Fig. 4) revealed several loops of ileum involved by regional enteritis. Medical treatment was recommended. The patient was uncooperative and decided to have treatment elsewhere. He returned for further care one year later with evidence of severe weight loss and marked progression of the lesion. The roentgen studies now disclosed

diffuse ileitis and ileojejunitis with some suggestions of fistula formation. Obstructive symptoms developed and surgery was done. An ileotransverse colostomy was done without exclusion. On the 9th postoperative day the patient expired suddenly from a pulmonary embolism.

Case 5:—I. S. A white female, age 30, had an ileotransverse colostomy with resection of the ileum, cecum and transverse colon for regional enteritis 18 months previously. The patient now complained of diarrhea, distention, crampy abdominal pains, nausea and vomiting. Roentgen studies (Fig. 5) revealed involvement of the ileum and transverse colon. Medical treatment did not improve the condition and the patient was hospitalized because of the obstructive symptoms. Treatment consisted of fluids, vitamins, antibiotics, and the use of the Miller-Abbott tube. The patient responded well to this management. Gradually the obstruction began to subside and the patient began to tolerate mouth feedings. Improvement continued on medical treatment and the general condition is satisfactory.

Case 6:—J. J. A white male, age 20, complained of diarrhea of two years' duration with considerable weight loss, with moderate anemia and blood in the evacuations. A roentgen study demonstrated extensive involvement of the jejunum and ileum and a second area of involvement in the terminal ileum. Obstructive symptoms developed. Surgery was considered. The patient responded to conservative measures for the intestinal obstruction. On a bland high protein diet, azulfidine and bentyl hydrochloride the patient has been doing satisfactorily for the past one year.

Case 7:—C. M. A white male, age 35, complained of abdominal cramps, fever, chills, nausea and vomiting. These symptoms had been present on and off for several years. There were brief periods when his condition improved and he had gained weight and was able to work. He was not hospitalized and studies of the upper digestive tract revealed (Fig. 6) changes in the duodenum and jejunum which suggested the presence of a granulomatous lesion of the duodenum suggestive of regional enteritis. Because of obstructive symptoms nausea, vomiting and increasing distention surgery was done. The duodenum and jejunum felt firm, contracted and rope-like. A gastrojejunostomy was done. The patient was fairly comfortable for two months. Then the symptoms returned. He was given a course of roentgen therapy with some relief of symptoms. Two weeks after the completion of his roentgen therapy symptoms returned. He was readmitted to another hospital with symptoms of intestinal obstruction. An exploratory laparotomy was done. A jejunal ulcer and a gastrojejunocolic fistula were found. A gastrectomy and resection of the jejunum and a portion of the transverse colon were done. The postoperative course was uneventful. A final diagnosis of subacute jejunitis was made. The patient made a good recovery. He regained his lost weight and assumed his normal activities. Five

somewhat similar patients with lesions involving the stomach and duodenum have been described by Comfort and his associates[3].

Case 8:—M. P. A white male, age 16, was seen with diarrhea, crampy abdominal pain, anemia, fever and weight loss. In 1948 the patient was operated upon for regional enteritis. A diffuse ileojejunitis was found so extensive that resection was deemed inadvisable. The patient's symptoms continued and became much more severe with more diarrhea, more weight loss. In 1954 he was reoperated because of obstructive symptoms. The small bowel was not so badly involved as five years previously. There were skip areas every four or five inches from the ligament of Treitz to and including the terminal ileum. An ileotransverse colostomy side-to-side was established between the terminal ileum and the midportion of the transverse colon. The patient continued to have diarrhea, abdominal pain, fever and obstructive symptoms. In October 1954 studies revealed extensive disease and the third operation was done. A resection of the terminal ileum, cecum and ascending colon was done. After a stormy postoperative period the patient made a good recovery. He still has a mild diarrhea but has regained his weight and strength.

Case 9:—N. T. A white male patient, age 40, developed very severe abdominal pain. The abdomen was distended, rigid and diffusely tender—although more so in the right lower abdomen. The patient gave a long history of atypical abdominal pains suggestive of duodenal ulcer. There were occasional episodes of diarrhea. A tentative diagnosis of a ruptured viscus was made and immediate surgery was recommended. A perforated terminal ileum involved by regional enteritis was found. An ileotransverse colostomy was done with exclusion. The patient recovered and later a resection of the involved ileum, cecum and transverse colon was done. Boyce[2] mentions three acute perforations in regional enteritis from the literature. Two of these patients died following surgery, one recovered.

Case 10:—M. W. A white male, age 43, was seen because of abdominal distention and crampy lower abdominal distress, nausea and vomiting. A diagnosis of small bowel obstruction was made. A history of an appendectomy six months ago was elicited. The patient had not been well since the appendectomy. He had had several episodes of intestinal obstruction since that time. The present attack of intestinal obstruction was treated conservatively and following its subsidence roentgen studies were done. The studies revealed a regional enteritis involving the terminal ileum. A side-to-side ileotransverse colostomy was done with exclusion. The patient made a good recovery following surgery.

Case 11:—H. L. A white male, age 24, developed pain in the right lower quadrant during an attack of intestinal "flu". On physical examination a sausage-shaped mass was felt in the lower right quadrant. The appendix had been removed some years previously. A roentgen study revealed a typical regional

enteritis involving the terminal ileum. A two-stage resection was done. The patient made a good recovery and has remained well.

Conclusions

Regional enteritis described a quarter of a century ago has increased greatly in frequency throughout the world.

The disease must be considered in the differential diagnosis of the patient with chronic diarrhea, with fever of unexplained origin or with abdominal or perirectal fistulas.

The patient with chronic regional enteritis may be treated medically when surgery is refused, when the disease process is too extensive for surgical resection or in recurrence after surgery.

Surgical treatment is necessary when medical therapy has failed to maintain reasonable health, for intestinal obstruction and other complications of the disease.

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REVERSE PERISTALSIS

A Report of Two Cases with X-ray Visualization of the Stomach at Time of Barium Enema

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and

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The purpose of this paper is to report two cases of reverse peristalsis manifested by x-ray visualization of the stomach at time of barium enema. These are presented because of the unusual nature of the condition.

Antiperistalsis is a mass movement directed cephalically which occurs normally in the duodenum and to a lesser extent in the ileum[1]. This is the reverse of the physiologic gradient that is normally present in the small intestine as postulated by Alvarez in his "law of the intestine"[2,3]. Alvarez believes that peristaltic movements take place along gradients independent of nervous mechanism, and that differences in the physiologic gradients in any two levels of the intestine determines the direction and swiftness of peristaltic movement[3].

Belching and vomiting are mild forms of reverse peristalsis. More massive antiperistalsis usually indicates profound functional derangement or actual organic disease. There are many well authenticated cases where enemas and suppositories have been vomited by the patient[3]. McLester[4] observed a barium enema (administered to a hysterical woman) travel from the colon to the stomach within 15 minutes.

Case Reports

Case 1:—N. S., a 54-year old white male, was admitted to the hospital 29 November 1954, because of a vague discomfort in the right lower quadrant of the abdomen. Appetite was good, there was no diarrhea, the abdomen was soft and no masses were palpable. General physical examination was negative. During barium enema there was easy reflux of the barium into the terminal ileum and by the time the initial film was taken a considerable amount of bowel was demonstrated containing barium. On the evacuation film barium was seen in the stomach and upper small intestine. All of this was thought to be reflux and no evidence of fistulous communication was demonstrated. On 1 December 1954, the upper gastrointestinal series was done. No abnormal communication between the stomach and small bowel could be noted and the gastrointestinal series was reported as showing no evidence of organic disease of the upper gastrointestinal tract. During January, 1955, the patient received a series of 10

electroshock treatments. Subsequently, a repeat barium enema failed to reveal any evidence of reverse peristalsis.

Case 2:—W. F.,* a 49-year old white female was first seen 7 November 1949, with the chief complaint of severe cramps in the lower abdomen. The patient had taken an enema the day before without relief. On physical examination she was found to be sensitive over the hypogastric and left iliac areas. Flat plate of the abdomen showed the kidneys to be normal in size and shape, no evidence of calculi, and no undue gaseous distention. A barium enema given on 10 November 1949, showed the colon to fill without evidence of obstruction. The ileocecal valve was patent and barium outlined the entire small bowel. Following evacuation, the stomach was well outlined with barium. The possibility of fistulous communication could not be excluded. On the following day an upper gastrointestinal series showed no evidence of fistulous communication between the stomach, small bowel and colon.

Comment

The resistance of a normal ileocecal sphincter may be overcome by a marked increase in pressure in the ascending colon and cecum, while a barium enema is being given for the purpose of examination. If, however, the opaque fluid runs easily and rapidly into the ileum in the absence of appreciable dilatation of the ascending colon, the sphincter may be looked upon as incompetent[5].

The problem of reverse peristalsis is twofold. First because no organic defect is found these patients are often labeled as psychoneurotics whereas actually they have a legitimate basis for their complaints. Disturbances of motility are much more frequent and more potent causes of digestive tract discomfort than abnormal secretory activity. Moderate departure from normal secretory activity does not as a rule interfere with the comfort of the average person, whereas in motor disturbances distress is readily experienced. Cardiospasm is an example. Even the distress of *globus hystericus* depends upon actual muscle spasm. A second consideration is that recognition of this entity may prevent unnecessary surgical exploration. A review of the literature shows a surprising number of cases in which the retrograde flow of barium seen during barium enema caused surgeons to operate for gastrocolic fistulas which were not found. In all cases of reverse peristalsis, however, an upper gastrointestinal series should be done.

Summary

Two cases of reverse peristalsis have been reported. In each instance the disturbance of gastrointestinal motility was manifested by x-ray visualization

*Patient of Dr. J. M. Perret, Sr.

of the stomach at the time of a barium enema. In neither case was a gastrocolic fistula demonstrable. In one of these two patients the pathognomonic x-ray signs of reverse peristalsis disappeared after electroshock therapy.

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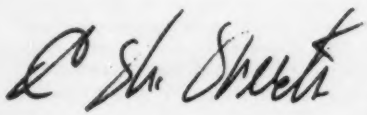
President's Message

The Coming Year

Periodic reflection and taking stock of where one stands in relationship to one's environment is probably not a bad practice at any time, but it is uniquely appropriate when entering upon the presidency of an organization. A question that comes to my mind is: Why do we have medical organizations? One obvious answer would seem to be the fact that we have common problems in certain areas of medicine and we hope that the organization will form a medium for the exchange of ideas leading to the best solution. This is, in a sense, a form of continuing medical education and its supervision carries with it definite responsibilities.

Our organization has three established channels, the annual and regional meetings, the annual postgraduate course and the journal, through which these responsibilities may be discharged and whereby an opportunity for work and participation is available to every member.

I am deeply appreciative of the honor accorded me in being elected President of the American College of Gastroenterology, and I hope that a philosophical approach to our tasks in the coming year will foster a sense of altruism and the probings of the inquiring mind so that our exchange of ideas will prove mutually profitable.



BOOK REVIEWS FOR GASTROENTEROLOGISTS

SYNOPSIS OF GASTROENTEROLOGY: Rudolph Schindler, M.D., F.A.C.P., Clinical Professor of Medicine (Gastroenterology), College of Medical Evangelists, Los Angeles, Calif., Consultant in Gastroenterology, Veterans Administration, Long Beach, Calif. 395 pages. Grune & Stratton, Inc., New York, N. Y., 1957. Price $7.75.

As stated by the author, "Synopsis of Gastroenterology" was written especially for the general practitioner and internist and to a great extent, embodies the personal experience of the author. The text is clear, concise, easily read and to the point. It is one book that is not cluttered up with illustrations which often detract rather than add value to the volume.

The section dealing with parasites, poisonous reptiles and insects, summarizes our present knowledge concerning the diagnosis and treatment involving the gastrointestinal tract.

General drug and dietotherapy complete the book, which also is concise and easily understood. An extensive index completes the text.

Dr. Schindler had written other books on gastrointestinal diseases and their diagnosis, but this one is the simplest and is highly recommended.

DIAGNOSIS AND TREATMENT OF CARDIOVASCULAR DISEASE: William D. Stroud, M.D., F.A.C.P., Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Past President, American Heart Association and Morris W. Stroud, III, M.D., Associate Professor of Medicine, Western Reserve University, Formerly Associate Editor, Circulation, Journal of the American Heart Association, aided by 60 celebrated authorities. Two volumes (looseleaf)—Volumes 1 and 2, 1702 pages, over 800 illustrations. F. A. Davis Company, Philadelphia, Pa., 1957. Price $35.00 per set.

The reviewer cannot do full justice in describing this monumental work on "Cardiovascular Disease" without waxing enthusiastic in praising the editors, coworkers and the publisher, who spared no time nor expense to make these volumes the most outstanding and instructive among books dealing with the heart and circulation.

The drawings, photographs, x-rays and electrocardiograms are classic. There are extensive references at the end of each chapter.

Among many new features, the reader will note a section on cardiac surgery, covering in detail the congenital and acquired lesions that are operable, ballistocardiography, electrocardiography, coronary artery disease and myocardial infarction, peripheral vascular disease and the newest diagnostic and therapeutic aids, plus the looseleaf form which will keep the text up to date whenever new developments occur.

"Cardiovascular Disease" is highly recommended as a must for the library of all physicians.

FUNDAMENTALS OF CLINICAL FLUOROSCOPY WITH ESSENTIALS OF ROENTGEN INTERPRETATION—2nd Revised Edition: Charles B. Storch, M.D., Associate Attending Roentgenologist, Radiodiagnostic Department, Beth-El Hospital, Brooklyn, N. Y. 305 pages, profusely illustrated. Grune & Stratton, New York, N. Y., 1957. Price $8.75.

The second edition by Dr. Storch has been thoroughly revised and brought up to date. Physicians who bought the first edition undoubtedly found many valuable suggestions. The reviewer is well pleased with this revised volume and has recommended it to his students as a "must".

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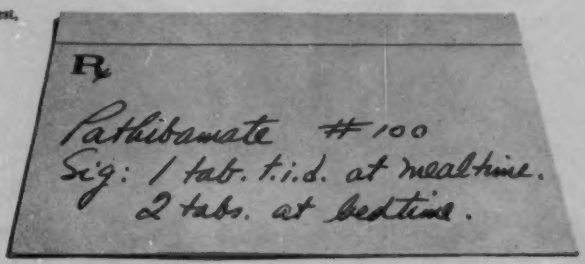

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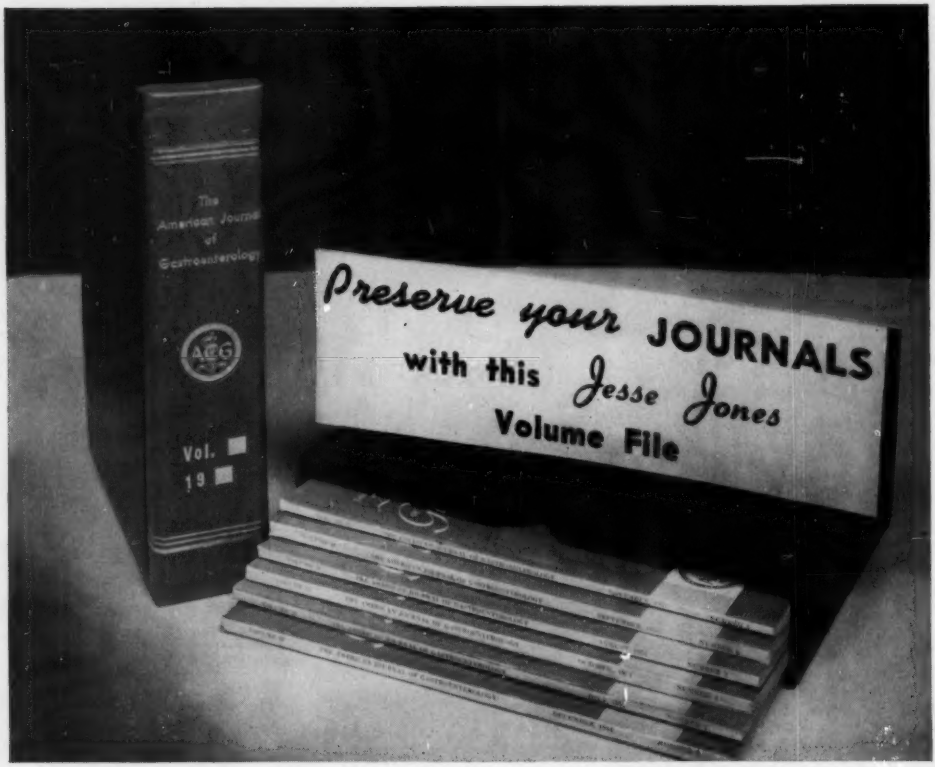

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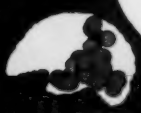

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Roentgenological healing of ulcer in 81% cases, relief of pain without analgesics in 92%, weight gains averaging 7.9 lbs. in 93%. Occult blood disappears from stools. No side effects, no after effects, no acid rebound.

This new therapy introduced from Holland (Pharmaceutische Fabriek Roter) is now available in the United States as Romach tablets, which contain finely particulated bismuth subnitrate (Romach process) combined with standard antacids.

Romach forms a protective coating of the ulcer bed, quickly relieving pain and also promoting rapid roentgenological healing.

Average dose, 2 tablets t.i.d., p.c. Available in boxes of 60, 150 and 660.

ROMACH

Write for Professional sample and literature.

ROR CHEMICAL CO. AJG—11
2268 First Ave., New York 35, N. Y

Please send me without obligation professional sample, and literature on Romach tablets.

..... M.D.

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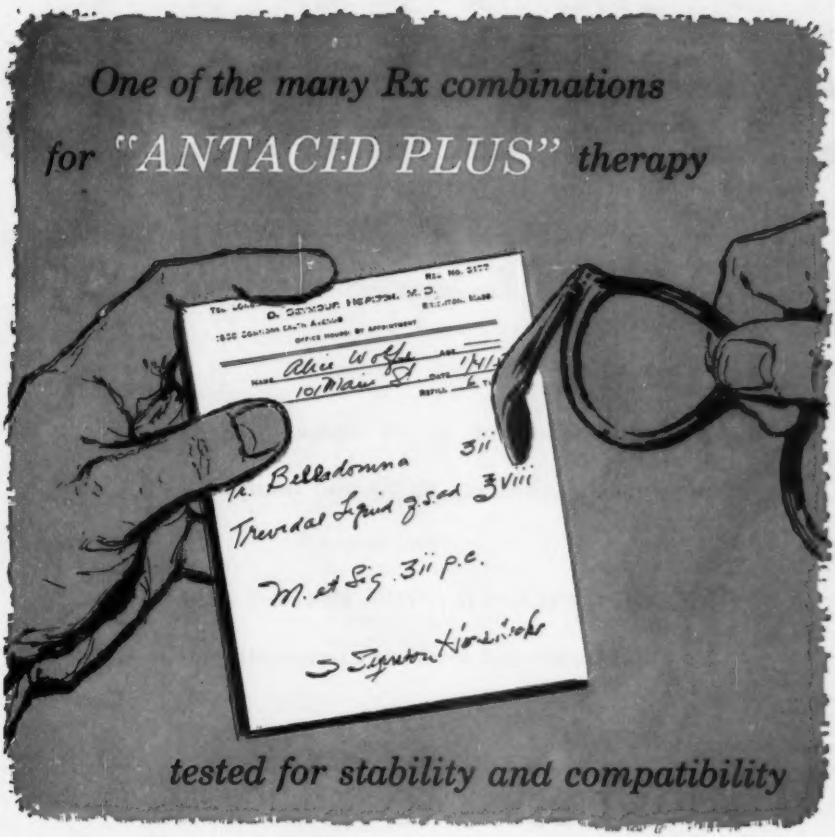
City ..... Zone ..... State .....


One of the many Rx combinations
for "ANTACID PLUS" therapy
Alice Wolfe
101 Main St
℞ Belladonna 3ii
Trevidal Liquid q.s.ad 3viii
M. et Sig. 3ii p.c.
tested for stability and compatibility

TREVIDAL® LIQUID

Because you often combine a liquid antacid with other medications, Trevidal Liquid is especially designed for stability and compatibilty in Rx combinations. It has been thoroughly tested with an antispasmodic, sedative, absorbent, antibacterial, costive, carminative, laxative, and digestant. A palatable and effective antacid providing balanced acid neutralization without bowel upsets, Trevidal Liquid makes it easier for you to individualize therapy for your patients by assuring stability and compatibility in your Rxs.

Each Teaspoonful (5 cc) contains:

Aluminum hydroxide	90 mg.
Calcium carbonate	105 mg.
Magnesium trisilicate	150 mg.
Magnesium carbonate	60 mg.
Egraine®*	45 mg.
Regonol®†	35 mg.

Available in 12-oz. bottles

*Binder from oat flour †Vegetable mucin

Organon INC.
ORANGE, N. J.

CONGENERS*

* *(Fusel oil — aldehydes — furfurals — acids — esters — etc.)*

These are present in all whiskey in varying amounts . . . creating flavor and bouquet.

In *HIGH CONCENTRATION*, however, congeners are undesirable and serve no therapeutic purpose.

LIGHT BLENDED WHISKIES...

lowest in congeners because of highly refined distillation processes . . . should therefore be of special interest to physicians when whiskey is prescribed.

Seagram • Calvert • Four Roses

405 LEXINGTON AVENUE NEW YORK 17, NEW YORK

PICK THE PIPERIDOL BEST FOR YOUR PATIENT

for pain⇄spasm of the upper G.I. tract

capsule
DACTIL®
Brand of Piperidolate HCl

visceral eutonic
relieves gastroduodenal and biliary pain⇄spasm —usually in 10 minutes

for peptic ulcer

tablet
PIPTAL®
Brand of Pipenzolate Methylbromide

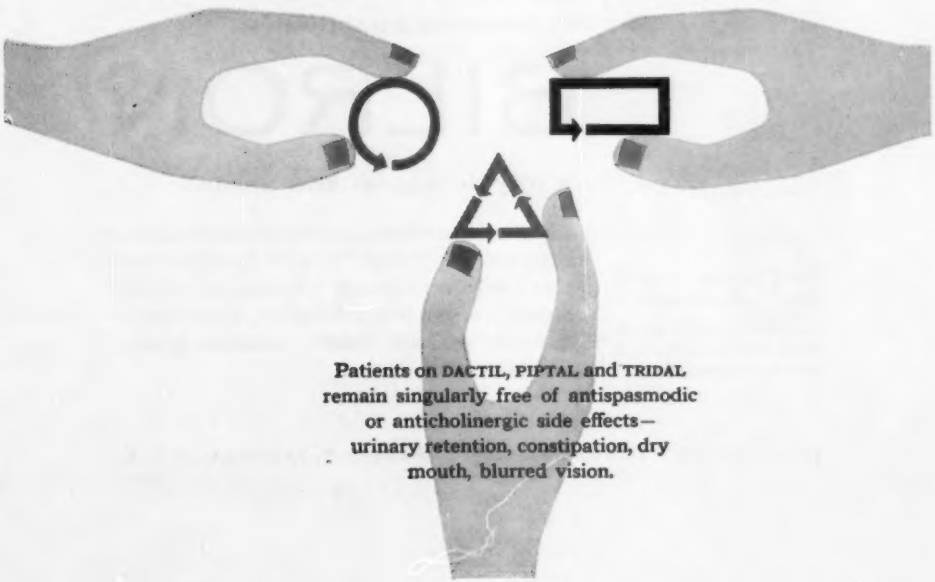
cholinolytic
normalizes motility *and* secretion; prolongs remissions, curbs recurrences

for generalized G.I. disorders

tablet
TRIDAL®
(DACTIL+PIPTAL—in one tablet)

rapid, prolonged relief *throughout the G.I. tract*

LAKESIDE



Patients on DACTIL, PIPTAL and TRIDAL remain singularly free of antispasmodic or anticholinergic side effects— urinary retention, constipation, dry mouth, blurred vision.

relieves after-eating distress

. . . chronic constipation

BILRON

(Iron Bile Salts, Lilly)

a physiological choleretic

. . . greatly increases the flow of bile of normal composition. 'Bilron' is acid insoluble and alkali soluble; therefore, it becomes physiologically active in the intestine, where bile is normally released. Gastric irritation is thus averted.

Usual dosage: 5 to 10 grains daily with meals.

Available in 2 1/2 and 5-grain tasteless pulvules at pharmacies everywhere.

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783017

for abnormal bowel function use

L. A.® Formula

It is important, when inducing normal bowel function, to supply a non-irritating bulk to the colon, especially in those cases in which it has been necessary to eliminate from the diet the high roughage foods containing irritating bulk (lignin and cellulose).

It has been shown[1] that the colon resumes a more normal peristaltic pattern[2] when it is supplied with a stool of medium soft consistency of sufficient bulk[3], especially if the indigestible portion of that bulk consists primarily of hemicellulose[4].

L. A. FORMULA is a vegetable concentrate of naturally occurring hemicelluloses. It is derived from blond psyllium seed by our special Ultra-Pulverization Process and simultaneously dispersed in lactose and dextrose. It provides just the moist, smooth, effective[5] bulk so essential to normal peristalsis.

Furthermore, L. A. FORMULA is undetectable in fruit juice and milk, pleasant tasting in water, and available in 7 and 14 ounce containers at significantly lower cost-to-patient prices. That's why we say L. A. FORMULA

. . . to normalize

1. Dolkart, R. E., Dentler, M., & Barrow, L. L., Illinois M. J., 90:286, 1946
2. Adler, H. F., Atkinson, A. J., & Ivy, A. C., Am. J. Digest. Dis., 8:197, 1941
3. Wozasek, O., & Steigman, F., Am. J. Digest. Dis., 9:423, 1942
4. Williams, R. D. & Olmsted, W. H., Ann. Int. Med., 10:717, 1936
5. Cass, L. J. & Wolf, L. P., Gastroenterology, 20:149, 1952

Formula: 50% plantago ovata coating dispersed in lactose and dextrose.

Made by BURTON, PARSONS & COMPANY *Since 1932*

Originators of Fine Hydrophilic Colloids

WASHINGTON 9, D. C.

put a new ending on this old tale

Old King Hal has many modern counterparts: executives who entertain . . . husbands who like "good eating," wives who serve "something different" . . . children who like "gooey" sweets. But for each the aftermath is often uncomfortable.

With Gelusil tablets or liquid, however, you quickly, soothingly relieve acute and chronic excessive gastric acidity! And Gelusil helps you manage the gnawing pain of peptic ulcer, too.

Gelusil stabilizes burning gastric acid within normal pH range, usually in minutes.

- *Gelusil works fast*
- *Gelusil is long-lasting*
- *Gelusil won't constipate*

Your patients get nightlong, sleep-assured protection with new formula Gelusil-Lac. By combining Gelusil's proven antacid action with the buffering effect of high-protein, low-fat milk solids, Gelusil-Lac *prevents* "middle-of-the-night" gastric pain!

there's no laxative in Gelusil . . . Gelusil needs no laxative

Gelusil®/Gelusil-Lac

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100 YEARS OF SERVICE TO THE MEDICAL PROFESSION